Clinical trial results:
A Randomised, Double-Blind, Placebo-Controlled, Dose-Response Study of the Efficacy and Safety of MEDI7352 in Subjects with Painful Diabetic Neuropathy

Summary

EudraCT number	2018-002523-42
Trial protocol	GB ES PL HU DK RO
Global end of trial date	29 June 2023

Results information

Result version number	v1
This version publication date	14 July 2024
First version publication date	14 July 2024

Trial information

Trial identification

Sponsor protocol code	D5680C00002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03755934
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	31 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 June 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the efficacy of MEDI7352 versus placebo on chronic pain in subjects with painful diabetic neuropathy (PDN) currently taking standard of care medication for their PDN pain.

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	19 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 62
Country: Number of subjects enrolled	Romania: 6
Country: Number of subjects enrolled	United Kingdom: 34
Country: Number of subjects enrolled	Hungary: 10
Worldwide total number of subjects	112
EEA total number of subjects	78

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	68
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 45 sites in 4 countries (the United Kingdom, Hungary, Poland, and Romania).

Pre-assignment

Screening details:

A total of 112 participants were randomized, of which 107 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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received intravenous (IV) placebo infusion matched to MEDI7352 during 12-week treatment period.

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

Dosage and administration details:

IV placebo infusion matched to MEDI7352 during 12-week treatment period.

Arm title	MEDI7352 Low Dose

Arm description:

Participants received IV MEDI7352 infusion during 12-week treatment period.

Arm type	Experimental
Investigational medicinal product name	MEDI7352
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV MEDI7352 given during a 12-week treatment period.

Arm title	MEDI7352 Medium Dose

Arm description:

Participants received IV MEDI7352 infusion during 12-week treatment period.

Arm type	Experimental

Investigational medicinal product name	MEDI7352
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV MEDI7352 given during a 12-week treatment period.

Arm title	MEDI7352 High Dose

Arm description:

Participants received IV MEDI7352 infusion during 12-week treatment period.

Arm type	Experimental
Investigational medicinal product name	MEDI7352
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV MEDI7352 given during a 12-week treatment period.

Number of subjects in period 1	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose
Started	54	6	16
Treated	54	4	14
Completed	40	4	12
Not completed	14	2	4
Physician decision	2	-	-
Consent withdrawn by subject	5	-	-
Adverse event, non-fatal	4	1	1
Unspecified	3	1	3

Number of subjects in period 1	MEDI7352 High Dose
Started	36
Treated	35
Completed	30
Not completed	6
Physician decision	1
Consent withdrawn by subject	1
Adverse event, non-fatal	3
Unspecified	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received intravenous (IV) placebo infusion matched to MEDI7352 during 12-week treatment period.	
Reporting group title	MEDI7352 Low Dose
Reporting group description:	
Participants received IV MEDI7352 infusion during 12-week treatment period.	
Reporting group title	MEDI7352 Medium Dose
Reporting group description:	
Participants received IV MEDI7352 infusion during 12-week treatment period.	
Reporting group title	MEDI7352 High Dose
Reporting group description:	
Participants received IV MEDI7352 infusion during 12-week treatment period.	

Reporting group values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose
Number of subjects	54	6	16
Age Categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	35	3	9
From 65-84 years	19	3	7
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	60.7	60.7	60.1
standard deviation	± 8.02	± 17.14	± 11.49
Sex: Female, Male Units: Participants			
Female	20	0	5
Male	34	6	11
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	2
White	53	6	14
More than one race	0	0	0
Unknown or Not Reported	1	0	0

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	54	6	16
Unknown or Not Reported	0	0	0

Reporting group values	MEDI7352 High Dose	Total	
Number of subjects	36	112	
Age Categorical Units: Participants			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	21	68	
From 65-84 years	15	44	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	60.1		
standard deviation	± 10.21	-	
Sex: Female, Male Units: Participants			
Female	15	40	
Male	21	72	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	2	
White	36	109	
More than one race	0	0	
Unknown or Not Reported	0	1	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	36	112	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received intravenous (IV) placebo infusion matched to MEDI7352 during 12-week treatment period.	
Reporting group title	MEDI7352 Low Dose
Reporting group description:	
Participants received IV MEDI7352 infusion during 12-week treatment period.	
Reporting group title	MEDI7352 Medium Dose
Reporting group description:	
Participants received IV MEDI7352 infusion during 12-week treatment period.	
Reporting group title	MEDI7352 High Dose
Reporting group description:	
Participants received IV MEDI7352 infusion during 12-week treatment period.	

Primary: Change From Baseline in Weekly Average of Average Daily Pain Score to Week 12

End point title	Change From Baseline in Weekly Average of Average Daily Pain Score to Week 12
End point description:	
Change from baseline to Week 12 in weekly average of average daily pain score is reported. Participants assessed their perceived daily average neuropathic pain over the previous 24 hours using an 11-point numerical rating scale (NRS), with 0 representing no pain and 10 representing the worst pain imaginable. Participants were instructed to assess their average daily pain at approximately the same time every morning, and to record the response in a subject diary (electronic patient-reported outcome [ePRO]). Modified intent-to-treat (mITT) population included all participants who received at least 1 dose of any double-blind study drug and have at least 1 daily NRS assessment while receiving the treatment.	
End point type	Primary
End point timeframe:	
Baseline (Day -7 to Day -1, inclusive) through Week 12	

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Unit on a score				
arithmetic mean (standard deviation)	-1.244 (± 1.7327)	-3.387 (± 1.9605)	-0.615 (± 1.0431)	-2.699 (± 2.0819)

Statistical analyses

Statistical analysis title	ANCOVA Analysis
Comparison groups	Placebo v MEDI7352 Low Dose

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0437 [1]
Method	ANCOVA
Parameter estimate	LS mean estimate
Point estimate	-1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.87
upper limit	-0.06
Variability estimate	Standard error of the mean
Dispersion value	0.961

Notes:

[1] - ANCOVA by dose using NRS baseline value and co-medication as covariates, with CFB to Week 12 (LOCF) as dependent variable was used to derive p-value.

Statistical analysis title	ANCOVA Analysis
Comparison groups	Placebo v MEDI7352 High Dose
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0009 [2]
Method	ANCOVA
Parameter estimate	LS mean estimate
Point estimate	-1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.19
upper limit	-0.58
Variability estimate	Standard error of the mean
Dispersion value	0.407

Notes:

[2] - ANCOVA by dose using NRS baseline value and co-medication as covariates, with CFB to Week 12 (LOCF) as dependent variable was used to derive p-value.

Statistical analysis title	ANCOVA Analysis
Comparison groups	Placebo v MEDI7352 Medium Dose
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1878 [3]
Method	ANCOVA
Parameter estimate	LS mean estimate
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	1.79

Variability estimate	Standard error of the mean
Dispersion value	0.541

Notes:

[3] - ANCOVA by dose using NRS baseline value and co-medication as covariates, with CFB to Week 12 (LOCF) as dependent variable was used to derive p-value.

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

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

End point description:

Change from baseline to Weeks 2, 4, 6, 8, 10, and 18 in weekly average of average daily pain score is reported. Participants assessed their perceived daily average neuropathic pain over the previous 24 hours using an 11-point NRS, with 0 representing no pain and 10 representing the worst pain imaginable. Participants were instructed to assess their average daily pain at approximately the same time every morning, and to record the response in a subject diary (ePRO). mITT population included all participants who received at least 1 dose of any double-blind study drug and have at least 1 daily NRS assessment while receiving the treatment. Here, 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, 4, 6, 8, 10, and 18

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Unit on a score				
arithmetic mean (standard deviation)				
Week 2 (n=53,4,14,35)	-0.385 (± 0.6863)	-1.089 (± 1.0258)	-0.311 (± 0.6285)	-0.540 (± 1.2503)
Week 4 (n=54,4,13,35)	-0.563 (± 1.0173)	-2.173 (± 1.4266)	-0.144 (± 0.9143)	-1.508 (± 1.5130)
Week 6 (n=50,4,13,34)	-0.955 (± 1.3236)	-2.458 (± 2.2156)	-0.578 (± 1.0715)	-2.044 (± 1.7916)
Week 8 (n=46,4,12,33)	-1.236 (± 1.6026)	-2.393 (± 2.0249)	-0.690 (± 1.2819)	-2.372 (± 2.0607)
Week 10 (n=44,4,12,33)	-1.418 (± 1.6274)	-2.595 (± 2.2003)	-0.712 (± 1.2164)	-2.629 (± 1.9943)
Week 18 (n=40,4,12,30)	-1.764 (± 1.8415)	-2.607 (± 2.2020)	-0.550 (± 1.2333)	-2.559 (± 2.1241)

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Percentage of participants with >=30% and >=50% decrease in weekly average of average daily pain score from baseline is reported. Participants assessed their perceived daily average neuropathic pain

over the previous 24 hours using an 11-point NRS, with 0 representing no pain and 10 representing the worst pain imaginable. Participants were instructed to assess their average daily pain at approximately the same time every morning, and to record the response in a subject diary (ePRO). mITT population included all participants who received at least 1 dose of any double-blind study drug and have at least 1 daily NRS assessment while receiving the treatment. Here, 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 4, 8, 12, and 18 (follow-up)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	13	35
Units: Percentage of participants				
number (not applicable)				
>=30%: Week 4 (n=54,4,13,35)	3.7	75.0	7.7	34.3
>=30%: Week 8 (n=46,4,12,33)	28.3	75.0	16.7	57.6
>=30%: Week 12 (n=43,4,12,33)	32.6	75.0	8.3	66.7
>=30%: Week 18 (n=40,4,12,30)	35.0	50.0	25.0	56.7
>=50%: Week 4 (n=54,4,13,35)	1.9	0	0	14.3
>=50%: Week 8 (n=46,4,12,33)	13.0	25.0	8.3	36.4
>=50%: Week 12 (n=43,4,12,33)	11.6	50.0	8.3	42.4
>=50%: Week 18 (n=40,4,12,30)	15.0	25.0	0	40.0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Galer Neuropathic Pain Scale (NPS)

End point title	Change From Baseline in Galer Neuropathic Pain Scale (NPS)

End point description:

Change from baseline to Weeks 4, 8, 12, 18 (follow-up) in Galer NPS total score is reported. The Galer NPS included 2 descriptors of pain, including intensity and unpleasantness, and 8 descriptors that assessed specific qualities of neuropathic pain: sharp, hot, dull, cold, sensitive, itchy, deep, and surface pain. Each of these 10 dimensions had a 0 to 10 NRS in which 0 is equal to no pain and 10 equals the most intense pain. mITT population included all participants who received at least 1 dose of any double-blind study drug and have at least 1 daily NRS assessment while receiving the treatment. 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 4, 8, 12, and 18 (follow-up)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	4	12	31
Units: Unit on a score				
arithmetic mean (standard deviation)				
Week 4 (n=48,4,11,31)	-13.333 (± 29.0461)	-5.750 (± 10.5317)	-10.727 (± 21.3967)	-26.387 (± 26.9922)
Week 8 (n=44,4,12,31)	-19.136 (± 31.5577)	-8.750 (± 18.2094)	-19.333 (± 23.7538)	-29.516 (± 32.3140)
Week 12 (n=39,4,11,29)	-24.385 (± 31.1081)	-28.750 (± 16.6808)	-22.000 (± 28.9379)	-34.586 (± 31.2622)
Week 18 (follow-up;n=36,4,11,29)	-25.722 (± 33.6151)	-23.000 (± 23.3095)	-27.909 (± 30.3725)	-25.414 (± 25.8947)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With 'Improved', 'Much Improved', or 'Very Much Improved' Status in Patient Global Impression of Change (PGIC)

End point title	Percentage of Participants With 'Improved', 'Much Improved', or 'Very Much Improved' Status in Patient Global Impression of Change (PGIC)

End point description:

Participants rated their overall improvement in health status using the PGIC. The PGIC consisted of a 7-point scale where 1 = very much improved and 7 = very much worse. The participants were asked the following question: How would you rate your overall improvement with treatment during the clinical study?, where the response options included the following: Very Much Improved, Much Improved, Minimally Improved, No Change, Minimally Worse, Much Worse, and Very Much Worse. mITT population included all participants who received at least 1 dose of any double-blind study drug and have at least 1 daily NRS assessment while receiving the treatment. 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 4, 8, 12, and 18 (follow-up)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	4	12	31
Units: Percentage of participants				
number (not applicable)				
Week 4: Improved (n=48,4,11,31)	50.0	50.0	45.5	41.9
Week 4: Much Improved (n=48,4,11,31)	2.1	25.0	27.3	29.0
Week 4: Very Much Improved (n=48,4,11,31)	2.1	0	0	6.5
Week 8: Improved (n=44,4,12,31)	36.4	25.0	58.3	41.9
Week 8: Much Improved (n=44,4,12,31)	31.8	50.0	41.7	38.7

Week 8: Very Much Improved (n=44,4,12,31)	2.3	0	0	6.5
Week 12: Improved (n=39,4,11,29)	48.7	0	54.5	44.8
Week 12 Much Improved (n=39,4,11,29)	28.2	75.0	36.4	41.4
Week 12: Very Much Improved (n=39,4,11,29)	5.1	25.0	0	10.3
Week 18: Improved (n=36,4,11,29)	36.1	25.0	27.3	31.0
Week 18: Much Improved (n=36,4,11,29)	25.0	50.0	54.5	41.4
Week 18: Very Much Improved (n=36,4,11,29)	11.1	25.0	9.1	13.8

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Daily Sleep Interference Scale (DSIS)

End point title	Change From Baseline in Daily Sleep Interference Scale (DSIS)

End point description:

Change from baseline to Weeks 4, 8, 12, and 18 (follow-up) in DSIS is reported. Participants assessed how their neuropathic pain interferes with their sleep using the DSIS. The DSIS is an 11-point Likert scale, with 0 indicating that pain did not interfere with sleep and 10 indicating that pain completely interfered with sleep. The DSIS was completed by the participants once a day (upon awakening) on a daily basis. mITT population included all participants who received at least 1 dose of any double-blind study drug and have at least 1 daily NRS assessment while receiving the treatment. 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 4, 8, 12, and 18 (follow-up)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	4	13	35
Units: Unit on score				
arithmetic mean (standard deviation)				
Week 4 (n=52,4,13,35)	-0.760 (± 1.1212)	-2.810 (± 2.6979)	-0.979 (± 1.7930)	-1.790 (± 1.5688)
Week 8 (n=46,4,12,33)	-1.417 (± 1.7654)	-3.143 (± 2.7430)	-1.127 (± 1.4907)	-2.373 (± 2.1368)
Week 12 (n=42,4,12,33)	-1.668 (± 2.1928)	-3.735 (± 2.7598)	-1.077 (± 1.4769)	-2.725 (± 2.2484)
Week 18 (follow-up;n=40,4,12,30)	-1.824 (± 2.2582)	-3.036 (± 2.6557)	-0.865 (± 1.2795)	-2.602 (± 2.4427)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 36-item Short-Form Health Survey (SF-36)

End point title	Change From Baseline in 36-item Short-Form Health Survey (SF-36)

End point description:

Change from baseline to Week 12 in SF-36 is reported. The SF-36 assesses 8 health concepts: 1) limitations in physical activities because of health problems (physical functioning); 2) limitations in social activities because of physical or emotional problems (social functioning); 3) limitations in usual role activities because of physical health problems (role physical); 4) bodily pain; 5) general mental health; 6) limitations in usual role activities because of emotional problems (role emotional); 7) vitality; and 8) general health perceptions. The items use Likert-type scales with either 5 or 6 points, or 2 or 3 points. Higher SF-36 scores indicate a better state of health. Score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). mITT population: all participants who received at least 1 dose of any double-blind study drug and have at least 1 daily NRS assessment while receiving treatment.

End point type	Secondary

End point timeframe:

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

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	4	12	29
Units: Unit on a score				
arithmetic mean (standard deviation)				
Physical Functioning	11.282 (± 17.0412)	21.248 (± 13.1526)	0.417 (± 19.7084)	12.759 (± 16.6141)
Role Physical	7.372 (± 18.0159)	28.125 (± 27.7169)	0.000 (± 37.3101)	6.681 (± 17.4338)
Bodily Pain	8.3 (± 20.51)	9.8 (± 22.75)	12.1 (± 23.11)	14.9 (± 17.30)
General Health	-2.6 (± 17.70)	-2.5 (± 5.00)	-5.3 (± 17.72)	0.0 (± 19.98)
Vitality	-0.160 (± 20.6039)	3.125 (± 16.5359)	-0.521 (± 17.7695)	-4.095 (± 24.0486)
Social Functioning	1.92 (± 19.772)	31.25 (± 23.936)	-1.04 (± 24.108)	9.05 (± 23.121)
Role Emotional	-1.923 (± 25.3248)	8.333 (± 31.9110)	-5.556 (± 34.8748)	-1.724 (± 19.9681)
Mental Health	-5.9 (± 21.82)	10.0 (± 20.41)	-1.3 (± 14.48)	-0.7 (± 18.41)

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants Taking any Rescue Medication

End point title	Proportion of Participants Taking any Rescue Medication

End point description:

Percentage of participants taking any rescue medication are reported. Participants were asked to record all rescue medications they take for neuropathic pain in a paper diary. mITT population included all participants who received at least 1 dose of any double-blind study drug and have at least 1 daily NRS assessment while receiving the treatment.

End point type	Secondary

End point timeframe:

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

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Percentage of participants				
number (not applicable)	13.0	0	14.3	8.6

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, diastolic blood pressure, systolic blood pressure, heart rate, and respiratory rate).

End point type	Secondary

End point timeframe:

Day 1 through 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants				
Blood pressure increased	0	0	0	1
Hypotension	0	0	0	1
Hypertension	1	0	0	0
Orthostatic hypertension	1	0	0	0
Orthostatic hypotension	3	0	0	0

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 population 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 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants				
Any TEAEs	30	4	10	23
Any TESAEs	1	0	0	0

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 population 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. Here, number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Day 1 through 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants				
Day 1 (n=54,4,14,35)	1	0	0	0
Week 4 (n=50,4,13,32)	0	0	1	0

Week 8 (n=45,4,12,32)	0	0	0	1
Week 12 (n=40,4,11,31)	1	0	0	1
Week 18 (follow-up;n=40,4,12,30)	0	0	1	0

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. Abnormal clinical laboratory parameters defined as any abnormal finding during analysis of hematology, clinical chemistry, coagulation, and urinalysis. Safety population 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 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants				
Alanine aminotransferase increased	0	0	2	0
Blood glucose decreased	0	0	1	1
Aspartate aminotransferase increased	0	0	1	0
Blood glucose increased	0	0	0	1
C-reactive protein increased	1	0	0	1
Coagulation test abnormal	0	0	0	1
Glomerular filtration rate decreased	0	0	0	1
White blood cells urine positive	0	0	0	1
Bacterial test positive	1	0	0	0
Blood bilirubin increased	1	0	0	0
Protein urine present	1	0	0	0
Urine analysis abnormal	1	0	0	0
Hypoglycaemia	1	0	1	1
Hypercholesterolaemia	0	0	0	1
Hyperglycaemia	1	0	1	0

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 TEAEs are reported. A complete physical examination (excluding the genitourinary examination, unless warranted) was performed. Safety population 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 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants	1	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Dorsiflexion Strength

End point title	Number of Participants With Abnormal Dorsiflexion Strength

End point description:

Number of participants with abnormal dorsiflexion strength is reported. Dorsiflexion strength is scored on 0-4 scale. The scale indicated 0 = normal power, 1 = mild weakness, 2 = moderate weakness, 3 = severe weakness, and 4 = paralysis. Safety population 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. Here, number of participants analyzed (N) denotes those participants who were assessed for strength and deep tendon reflexes assessment.

End point type	Secondary

End point timeframe:

Day 1 through 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	4	12	30
Units: Participants				
Mild Weakness	9	0	7	18
Moderate Weakness	8	0	0	2
Severe Weakness	0	0	0	0

Paralysis	0	0	0	0

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Number of participants with clinically significant findings in neurological examination is reported. Safety population 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 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Deep Tendon Reflex (Knee and Ankle)

End point title	Number of Participants With Abnormal Deep Tendon Reflex (Knee and Ankle)

End point description:

Number of participants with deep tendon reflex are reported. Deep tendon reflex (knee and ankle) strength is scored on 0-4 scale. The scale indicated 0 = normal, 1 = ankle reflex reduced, 2 = ankle reflex absent, 3 = ankle reflex absent and knee reflex reduced, and 4 = all reflexes (both ankle and knee) absent. Safety population 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. Here, number of participants analyzed (N) denotes those participants who were assessed for strength and deep tendon reflexes assessment.

End point type	Secondary

End point timeframe:

Day 1 through 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	4	12	30
Units: Participants				
Ankle reflex reduced	5	2	2	3
Ankle reflex absent	4	0	1	5
Ankle reflex absent and knee reflex reduced	11	1	3	13
All reflexes absent	15	0	6	5

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Neuropathy Score-Nurse (TNSn)

End point title	Change From Baseline in Total Neuropathy Score-Nurse (TNSn)

End point description:

TNSn, a semi-quantitative clinical assessment of peripheral nervous system function, was administered at baseline (Screening), Day 1, Weeks 2, 4, 6, 8, 10, 12, and 18. The TNSn provides for assessment of motor symptom, autonomic symptom, pin sensibility, and vibration sensibility score. Each neuropathy item is scored on a 0–4 scale. The scores are summed to obtain a total score. Higher total scores correlate with more severe neuropathy. The arbitrary numbers 99.999 and 99999 signified mean and standard deviation, respectively, not reported as no participants were evaluable for the arm. The arbitrary numbers 999.99 signified standard deviation not reported as only one participant was evaluable for this arm. Safety population included all participants who received at least 1 dose of any double-blind study drug and were analysed according to the treatment they actually received. Here, number analysed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day -45 to -1), pre-dose on Day 1, Weeks 2, 4, 6, 8, 10, 12, and 18/early termination

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	4	13	34
Units: Unit on a score				
arithmetic mean (standard deviation)				
Day 1 (n=4,0,0,1)	-0.25 (± 0.957)	99.999 (± 99999)	99.999 (± 99999)	1.00 (± 999.99)
Week 2 (n=48,4,13,34)	-0.54 (± 1.304)	-1.25 (± 1.258)	0.00 (± 1.354)	-0.94 (± 2.117)
Week 4 (n=50,4,13,32)	-0.90 (± 1.982)	-2.50 (± 3.786)	-0.85 (± 1.819)	-1.19 (± 1.891)
Week 6 (n=45,4,12,33)	-1.40 (± 2.071)	-0.75 (± 2.872)	-1.00 (± 1.859)	-1.85 (± 2.093)
Week 8 (n=45,4,12,32)	-1.40 (± 2.082)	-2.50 (± 3.000)	-0.92 (± 1.881)	-1.84 (± 2.665)

Week 10 (n=40,4,12,31)	-1.90 (± 2.458)	-2.00 (± 3.916)	-1.67 (± 1.435)	-2.45 (± 3.042)
Week 12 (n=40,4,12,30)	-1.73 (± 2.562)	-2.25 (± 2.062)	-2.17 (± 1.899)	-2.53 (± 2.515)
Week 18 (n=40,4,12,30)	-2.00 (± 2.631)	-2.50 (± 3.512)	-2.17 (± 2.329)	-2.30 (± 3.053)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Investigator Reported Significant Changes From Baseline in Motor and Sensory Nerve Conduction

End point title	Number of Participants With Investigator Reported Significant Changes From Baseline in Motor and Sensory Nerve Conduction

End point description:

Motor and sensory nerve conduction studies were performed in relevant lower and upper limb nerves (sural, peroneal, median/ulnar, fibular, and tibial nerves) wherein amplitude, peak latency, conduction velocity, and duration of nerve action potentials were recorded. Safety population included all participants who receivedat 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 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants	2	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With at Least One Concomitant Medication

End point title	Number of Participants With at Least One Concomitant Medication

End point description:

Number of participants with at least one concomitant medication is reported. A concomitant medication is defined as any medication continuing or starting after first dose of study medication. Safety population 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 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants	54	4	14	35

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Injection Site Reaction

End point title	Number of Participants With Injection Site Reaction

End point description:

Number of participants with injection site reaction is reported. Safety population 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 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants	1	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Total Nerve Growth Factor (NGF) Concentrations

End point title	Serum Total Nerve Growth Factor (NGF) Concentrations

End point description:

Serum concentrations of total NGF in ADA positive or negative participants are reported. Safety population 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 outcome measure. Here, number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Pre-dose: Day 1 (baseline), Weeks 2, 4, 6, 8; Week 10 (Day 70; pre-dose, immediately before end of infusion, 8 hours post infusion start), Day 71 (post 24 hours of Day 70 infusion start), Weeks 11, 12 (approximately same time of day as Week 10 infusion)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	0[4]	0[5]	31
Units: pg/mL				
arithmetic mean (standard deviation)				
Day 1 (n=30,0,0,31)	52.303 (± 11.6178)	()	()	65.687 (± 60.4036)
Week 2 (n=29,0,0,29)	62.613 (± 15.1088)	()	()	2384.760 (± 1989.0309)
Week 4 (n=29,0,0,29)	78.209 (± 92.0122)	()	()	2213.699 (± 2408.3112)
Week 6 (n=27,0,0,29)	64.661 (± 18.6478)	()	()	2361.855 (± 2645.8141)
Week 8 (n=26,0,0,29)	63.291 (± 16.5332)	()	()	1992.129 (± 2507.9826)
Week 10 (pre-dose; n=25,0,0,28)	173.383 (± 563.8921)	()	()	1681.073 (± 2455.0666)
Week 10 (before end of infusion; n=25,0,0,28)	57.308 (± 13.3588)	()	()	1992.756 (± 2968.1285)
Week 10 (8 hours post-dose; n=25,0,0,28)	177.323 (± 554.8131)	()	()	2012.384 (± 2795.8138)
Week 10 (post 24 hours; n=24,0,0,28)	222.980 (± 772.9408)	()	()	1849.835 (± 2671.9526)
Week 11 (n=25,0,0,26)	59.441 (± 13.6892)	()	()	1743.100 (± 2621.0687)
Week 12 (n=25,0,0,28)	63.416 (± 18.4243)	()	()	1710.966 (± 2838.0975)

Notes:

[4] - Due to change in total NGF assay during study course, participants from this arm are not analysed.

[5] - Due to change in total NGF assay during study course, participants from this arm are not analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Infusion Reaction

End point title	Number of Participants With Infusion Reaction

End point description:

Number of participants with infusion reaction is reported. Safety population 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 20.42 weeks (maximum observed duration)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	4	14	35
Units: Participants	0	0	0	2

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 positive ADA to MEDI7352 are reported. Treatment-induced ADA positive is defined as ADA negative at baseline and positive at least 1 post-baseline assessment. Treatment-boosted ADA positive is defined as ADA positive at baseline with pre-existing titer boosted by 4-fold or greater during the study period. Persistent positive is defined as ADA negative at baseline and positive at least 2 post-baseline assessments (with >= 16 weeks between first and last positive) or ADA positive at last post-baseline assessment. Transiently positive is defined as ADA negative at baseline and at least one post-baseline ADA positive measurement and not fulfilling the conditions for persistently positive. Safety population 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. Here, number of participants analyzed (N) denotes those participants who had adequate ADA sample.

End point type	Secondary

End point timeframe:

Pre-dose at baseline (Day -45 to -1) and Study Weeks 2, 4, 8, 10, 12, and 18 (follow-up)

End point values	Placebo	MEDI7352 Low Dose	MEDI7352 Medium Dose	MEDI7352 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	4	14	35
Units: Participants				
Treatment-induced ADA	0	3	7	28
Treatment-boosted ADA	0	0	1	1
Persistently positive ADA	0	3	6	26
Transiently positive ADA	0	0	1	2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 through 20.42 weeks (maximum observed duration)

Adverse event reporting additional description:

Safety population 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	Placebo

Reporting group description:

Participants received intravenous (IV) placebo infusion matched to MEDI7352 during 12-week treatment period.

Reporting group title	MEDI7352 High Dose

Reporting group description:

Participants received IV MEDI7352 during 12-week treatment period.

Reporting group title	MEDI7352 Medium Dose

Reporting group description:

Participants received IV MEDI7352 during 12-week treatment period.

Reporting group title	MEDI7352 Low Dose

Reporting group description:

Participants received IV MEDI7352 during 12-week treatment period.

Serious adverse events	Placebo	MEDI7352 High Dose	MEDI7352 Medium Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Lung abscess			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MEDI7352 Low Dose		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from	0		

adverse events			
Infections and infestations			
Lung abscess			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	MEDI7352 High Dose	MEDl7352 Medium Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 54 (55.56%)	23 / 35 (65.71%)	10 / 14 (71.43%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Orthostatic hypertension			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Lymphoedema			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	2
Hypotension			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Orthostatic hypotension			
subjects affected / exposed	3 / 54 (5.56%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Injection site reaction			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Facial pain			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Catheter site swelling			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Gravitational oedema			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 54 (1.85%)	1 / 35 (2.86%)	1 / 14 (7.14%)
occurrences (all)	1	1	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Bruxism			

subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 54 (1.85%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Blood glucose increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Blood glucose decreased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Coagulation test abnormal			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
White blood cells urine positive			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Bacterial test positive			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Lymph node palpable			

subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Protein urine present			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Urine analysis abnormal			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 54 (5.56%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Infusion related reaction			
subjects affected / exposed	0 / 54 (0.00%)	2 / 35 (5.71%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
Nail injury			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Repetitive strain injury			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			

subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	2
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Allodynia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Burning sensation			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	2 / 54 (3.70%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 54 (1.85%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Orthostatic intolerance			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	5 / 54 (9.26%)	1 / 35 (2.86%)	1 / 14 (7.14%)
occurrences (all)	9	1	2
Sensory disturbance			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Diabetic neuropathy			
subjects affected / exposed	2 / 54 (3.70%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Carpal tunnel syndrome			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Eye haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Conjunctivitis allergic			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Retinal haemorrhage			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Change of bowel habit			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Nausea			

subjects affected / exposed	2 / 54 (3.70%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	1
Mouth ulceration			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Frequent bowel movements			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	5 / 54 (9.26%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	6	1	0
Constipation			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Melaena			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia oral			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0

Dermatitis contact			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Skin burning sensation			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Lichenification			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hand dermatitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Urinary tract inflammation			
subjects affected / exposed	1 / 54 (1.85%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
Musculoskeletal discomfort			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	4 / 54 (7.41%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	4	0	0
Soft tissue mass			

subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	2 / 54 (3.70%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Muscle twitching			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	1 / 54 (1.85%)	2 / 35 (5.71%)	0 / 14 (0.00%)
occurrences (all)	1	3	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Pain in jaw			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 54 (5.56%)	4 / 35 (11.43%)	0 / 14 (0.00%)
occurrences (all)	3	5	0
Nasopharyngitis			
subjects affected / exposed	11 / 54 (20.37%)	2 / 35 (5.71%)	0 / 14 (0.00%)
occurrences (all)	11	3	0
Urinary tract infection			
subjects affected / exposed	2 / 54 (3.70%)	1 / 35 (2.86%)	2 / 14 (14.29%)
occurrences (all)	3	1	2
Acute sinusitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Herpes simplex			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0

Viral upper respiratory tract infection			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection bacterial			
subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 54 (1.85%)	1 / 35 (2.86%)	1 / 14 (7.14%)
occurrences (all)	3	1	1
Decreased appetite			
subjects affected / exposed	0 / 54 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 35 (2.86%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			

subjects affected / exposed	1 / 54 (1.85%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1

Non-serious adverse events	MEDI7352 Low Dose		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Orthostatic hypertension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lymphoedema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Orthostatic hypotension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Injection site reaction			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Facial pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Catheter site swelling			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Feeling hot			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gravitational oedema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Bruxism			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Blood glucose increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Blood glucose decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Alanine aminotransferase increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Coagulation test abnormal				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Glomerular filtration rate decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
White blood cells urine positive				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Bacterial test positive				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Blood bilirubin increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Lymph node palpable				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Protein urine present				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Urine analysis abnormal				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood pressure increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infusion related reaction			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nail injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Repetitive strain injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Ventricular extrasystoles			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Atrial fibrillation			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	4		
Allodynia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Burning sensation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Orthostatic intolerance			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	24		
Sensory disturbance			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Diabetic neuropathy			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Carpal tunnel syndrome			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Eye disorders			
Eye irritation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Eye haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Conjunctivitis allergic			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Conjunctival hyperaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Retinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Change of bowel habit			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Mouth ulceration			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Frequent bowel movements			

subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Food poisoning			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Abdominal discomfort			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Melaena			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoaesthesia oral			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dermatitis contact			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Erythema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin burning sensation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Lichenification			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hand dermatitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Urinary tract inflammation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Musculoskeletal discomfort			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Soft tissue mass			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Muscle twitching			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pain in jaw			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Acute sinusitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Eye infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Herpes simplex			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hordeolum			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tooth abscess			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Urinary tract infection bacterial			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hypercholesterolaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 May 2019	Added assessments of strength (dorsiflexion) and deep tendon reflexes (knee and ankle). Changed terminology from "cohort" to "stage". Added contraception guidance as an appendix. Modified the exclusion criteria to clarify that bilateral ankle radiographs were required at screening only if the participant had clinically significant sensory impairment. Modified the exclusion criteria to exclude participants with hemoglobin A1C (HbA1C) greater than 8.5% (formerly 8.0%). Specified that QuantiFERON tuberculosis (TB) testing was to be performed for all participants. Added a provision that, if necessary, the randomisation transaction in interactive web response system (IWRS) could be performed on Day -1. To avoid undue pressure on the participants, removed language that instructed the investigator to make every reasonable attempt to keep participants in the study. Added option for the sponsor to provide sterile water for injection and sodium chloride 0.9% solution for infusion if the site was unable to supply these. Noted that investigational product (IP) kit/code numbers were not to be recorded in the electronic case report form (eCRF). Removed the requirement that smoking habits were to remain unchanged for the duration of the study. Clarified that screening and Day 1 blood pressure assessments taken to assess orthostasis were to be measured in a supine (not sitting) position prior to the standing assessments. Clarified that urine pregnancy tests were to be performed in all women who were not surgically sterile. Specified that the sleep biosensor was to be worn on the nondominant wrist. Revised the list of sleep endpoints that the biosensor was capable of recording and analysing. Removed references to a clinical monitoring plan. Removed "Medimmune" from the sponsor name. Corrected typographical errors.
21 February 2020	Modified exclusion criteria to clarify that participants with a documented or suspected history of excessive alcohol usage or recreational drug usage should be evaluated at screening using appropriate quantitative or semi-quantitative methodologies according to local standards of accepted medical or psychiatric practice. Modified all instances of physical examinations to include physical and neurological examinations. Clarified that if the infusion was slowed or interrupted, the total infusion time should not exceed 4 hours at room temperature. Clarified that the timing of ECGs on Day 1 was relative to the start of IP administration. Added C-reactive protein to the serum chemistry tests to be performed. Modified the modified intent-to-treat population to include all randomised participants who received at least 1 dose of double-blind study medication and had at least 1 post-baseline (BL) NRS assessment.
01 October 2020	Modified doses used in Stage 3 of the study to include 10, 50, 150 and 450 µg/mL. Clarified the timing windows, namely for all vital signs, pharmacokinetic (PK), pharmacodynamic (PD), exploratory soluble biomarker sampling. Updated Clinical Experience from the most recent data safety cut-off of 23 April 2020. Modified the description of when participants in Stage 3 were to be randomly assigned to treatment of MEDI7352 or placebo. Modified the study design figure to include 10, 50, 150, and 450 µg/mL dose levels. Clarified the New York Heart Association (NYHA) exclusion criteria. Updated the number of study sites. Updated the study duration timing. Clarified who was to be included as an early terminated participant. Removed the futility analysis and clarified the naming of the Interim Analysis Review Committee to review the data for the interim analysis.

04 December 2020	Added a fourth stage to the study and updated the number of participants to be included in each stage. Modified doses used in Stage 2 to 4 of the study. Clarified the timing windows, namely for all vital signs, PK, PD, exploratory soluble biomarker sampling. Updated Clinical Experience from the most recent data safety cut-off of 23 April 2020. Modified the description about the timing of randomization before Stage 3. Modified the study design figure to include the appropriate dosing during the 4 stages of the study. Modified the sample size description and number of participants needed in the study. Updated the efficacy analysis to include a supplementary analysis using an adaptive MCP-Mod method. Updated when participants could be replaced to the third and fourth stages of the study. Clarified the NYHA exclusion criteria. Updated the number of study sites. Updated the study duration. Clarified who was to be defined as an early terminated participant.
26 October 2021	Updated clinical experience with data from the completed and ongoing clinical studies as of 01 June 2021 in line with the updated investigator's brochure (Edition 6, dated 13 October 2021). Added text to exclusion criteria #11 to indicate that bilateral radiographs taken to evaluate osteoarthritis severity and exclude neuropathic arthropathy should include feet as well as ankles. Modified the definition of hypertension in exclusion criteria #27. Modified the HbA1C limit in exclusion criteria #29, from 8.5% to 10.0%. Evaluation of a cartilage degradation marker, urine C-terminal cross-linked telopeptide of type II collagen, was added. Corresponding changes were made to the exploratory endpoint describing soluble and genomic biomarkers to include this marker, with additional changes to the schedule of events and to text describing procedures at the appropriate visits. Adverse events of special interest (AESI) were added to align AESIs across studies per participant safety recommendations.
13 April 2022	Broadened electrocardiogram (ECG) language to allow paper ECGs as an alternative to digital ECGs. Clarified that the principal investigator's assessment of each ECG was to be recorded in the eCRF as normal, abnormal and clinically significant, or abnormal and not clinically significant. Clarified that urine samples for CTX-II biomarkers should only be collected from participants who had a baseline sample collected at the screening visit. Clarified the details relating to the interim analysis after completion of stage 3. Provided additional details of vital signs capture, particularly with regard to the use of a supine or sitting position.

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.

Dose-response relationship outcome was not evaluated by MCP-MOD because of insufficient number of doses. Study was prematurely terminated due to longer enrolment time. PK data analysed using population PK method; reported as separate report.

Notes: