Clinical trial results:
A Phase 2a, Randomized, Double-Blind, Placebo-Controlled Trial of the Efficacy and Safety of LEVI-04 in Patients with Osteoarthritis of the Knee

Summary

EudraCT number	2021-006540-28
Trial protocol	CZ DK
Global end of trial date	20 May 2024

Results information

Result version number	v1 (current)
This version publication date	12 September 2025
First version publication date	12 September 2025

Trial information

Trial identification

Sponsor protocol code	LEVI-04-21-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05618782
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Levicept Ltd
Sponsor organisation address	Innovation House, Discovery Park, Ramsgate Road, Sandwich, United Kingdom, CT13 9ND
Public contact	Debbie Dutton , Levicept Ltd , 44 07430695385, info@levicept.com
Scientific contact	Claire Herholdt, Levicept Ltd , 44 07875737516, claire@levicept.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	19 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 May 2024
Global end of trial reached?	Yes
Global end of trial date	20 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of LEVI-04 (multiple doses) compared to placebo in reducing pain due to knee OA.

Protection of trial subjects:

Rescue medication (paracetamol, up to 4000mg/day) was provided, to be used if necessary.

Background therapy:

Rescue medication (paracetamol, up to 4000mg/day) was provided, to be used if necessary.

Evidence for comparator:

Saline vehicle was used as placebo and was indistinguishable from active once prepared for administration.

Actual start date of recruitment	19 October 2022
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: 81
Country: Number of subjects enrolled	Czechia: 143
Country: Number of subjects enrolled	Denmark: 211
Country: Number of subjects enrolled	Hong Kong: 66
Country: Number of subjects enrolled	Moldova, Republic of: 17
Worldwide total number of subjects	518
EEA total number of subjects	435

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)	236
From 65 to 84 years	282
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 19 October 2022 and 23 October 2023 518 participants were enrolled across 13 clinical research centers located in Denmark, Hong Kong, Poland, Moldova and Czech Republic.

Pre-assignment

Screening details:

1598 participants were screened to enroll 518. Screening period included a diary run-in period; participants had to record a minimum of 4/10 daily pain score. Participants also had to record a minimum of 20/50 points on the WOMAC pain subscore at screening and randomization visits, with at least 48 hours washout of other analgesics.

Period 1

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

Blinding implementation details:

Randomization performed using a central IVR. There was an unblinded pharmacist at each site to make up the infusions, and an unblinded monitor to perform drug accountability. Once made up, active infusions were indistinguishable from placebo. These roles had to be independent of any other trial activities. All other personnel were blinded to treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	LEVI-04 0.3mg/kg

Arm description:

LEVI-04 0.3 mg/kg intravenous infusion

Arm type	Experimental
Investigational medicinal product name	LEVI-04
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

LEVI-04 solution diluted with 5% dextrose to make up 0.3mg/kg infusion via saline drip over 30 minutes, once monthly.

Arm title	LEVI-04 1.0mg/kg

Arm description:

LEVI-04 1.0 mg/kg intravenous infusion

Arm type	Experimental
Investigational medicinal product name	LEVI-04
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

LEVI-04 solution diluted with 5% dextrose to make up 1.0 mg/kg infusion via saline drip over 30 minutes, once monthly.

Arm title	LEVI-04 2.0 mg/kg

Arm description:	
LEVI-04 2.0 mg/kg intravenous infusion	
Arm type	Experimental
Investigational medicinal product name	LEVI-04
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use
Dosage and administration details:	
LEVI-04 solution diluted with 5% dextrose to make up 2.0 mg/kg infusion via saline drip over 30 minutes, once monthly.	
Arm title	Placebo
Arm description:	
Placebo comparator (saline vehicle)	
Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous drip use
Dosage and administration details:	
Intravenous infusion of a saline drip over 30 minutes, once monthly	

Number of subjects in period 1	LEVI-04 0.3mg/kg	LEVI-04 1.0mg/kg	LEVI-04 2.0 mg/kg
Started	130	130	129
Completed	120	121	118
Not completed	10	9	11
Physician decision	1	1	1
Consent withdrawn by subject	5	4	5
not known	-	1	-
Adverse event, non-fatal	3	2	4
Lost to follow-up	1	1	1
Protocol deviation	-	-	-

Number of subjects in period 1	Placebo
Started	129
Completed	116
Not completed	13
Physician decision	-
Consent withdrawn by subject	7
not known	-
Adverse event, non-fatal	4
Lost to follow-up	-

Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	LEVI-04 0.3mg/kg
Reporting group description: LEVI-04 0.3 mg/kg intravenous infusion	
Reporting group title	LEVI-04 1.0mg/kg
Reporting group description: LEVI-04 1.0 mg/kg intravenous infusion	
Reporting group title	LEVI-04 2.0 mg/kg
Reporting group description: LEVI-04 2.0 mg/kg intravenous infusion	
Reporting group title	Placebo
Reporting group description: Placebo comparator (saline vehicle)	

Reporting group values	LEVI-04 0.3mg/kg	LEVI-04 1.0mg/kg	LEVI-04 2.0 mg/kg
Number of subjects	130	130	129
Age categorical			
between ≥40 and ≤80 years of age			
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)	68	55	67
From 65-84 years	62	75	62
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	67	80	69
Male	63	50	60

Reporting group values	Placebo	Total	
Number of subjects	129	518	
Age categorical			
between ≥40 and ≤80 years of age			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	

Adults (18-64 years)	46	236	
From 65-84 years	83	282	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	76	292	
Male	53	226	

End points

End points reporting groups	
Reporting group title	LEVI-04 0.3mg/kg
Reporting group description: LEVI-04 0.3 mg/kg intravenous infusion	
Reporting group title	LEVI-04 1.0mg/kg
Reporting group description: LEVI-04 1.0 mg/kg intravenous infusion	
Reporting group title	LEVI-04 2.0 mg/kg
Reporting group description: LEVI-04 2.0 mg/kg intravenous infusion	
Reporting group title	Placebo
Reporting group description: Placebo comparator (saline vehicle)	

Primary: WOMAC Pain Least Squares Mean Change from Baseline	
End point title	WOMAC Pain Least Squares Mean Change from Baseline
End point description: LSM Change from baseline in WOMAC pain subscore, LEVI-04 versus Placebo	
End point type	Primary
End point timeframe: Baseline to Week 17	

End point values	LEVI-04 0.3mg/kg	LEVI-04 1.0mg/kg	LEVI-04 2.0 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	130	129	129
Units: Subjects	130	130	129	129

Statistical analyses

Statistical analysis title	LSM WOMAC Pain LEVI-04 0.3mg/kg
Statistical analysis description: Least Squares (LS) Mean Difference Change from Baseline to Week 17 in Standardized WOMAC Pain Subscale Score compared to placebo	
Comparison groups	LEVI-04 0.3mg/kg v Placebo
Number of subjects included in analysis	259
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.23

Statistical analysis title	WOMAC Pain LEVI-04 1mg/kg
Statistical analysis description:	
LSM Difference in WOMAC Pain, Change from Baseline to Week 17, LEVI-04 1mg/kg versus Placebo	
Comparison groups	LEVI-04 1.0mg/kg v Placebo
Number of subjects included in analysis	259
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.23

Statistical analysis title	WOMAC Pain LEVI-04 2mg/kg
Statistical analysis description:	
LSM Difference in WOMAC Pain, Change from Baseline to Week 17, LEVI-04 2mg/kg versus Placebo	
Comparison groups	LEVI-04 2.0 mg/kg v Placebo
Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	-0.35
Variability estimate	Standard error of the mean
Dispersion value	0.23

Secondary: WOMAC Physical Function	
End point title	WOMAC Physical Function
End point description: Least Squares Mean Change from Baseline versus Placebo	
End point type	Secondary
End point timeframe: Baseline to Week 17	

End point values	LEVI-04 0.3mg/kg	LEVI-04 1.0mg/kg	LEVI-04 2.0 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	119	116	113
Units: Subjects	118	119	116	113

Statistical analyses

Statistical analysis title	WOMAC Physical Function, LEVI-04, 1mg/kg
Statistical analysis description: LSM Change from baseline to week 17 versus placebo	
Comparison groups	LEVI-04 1.0mg/kg v Placebo
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	-0.21
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	WOMAC Physical Function, LEVI-04, 0.3mg/kg
Statistical analysis description: Womac Physical function, Least Squares Mean change from baseline versus placebo	
Comparison groups	LEVI-04 0.3mg/kg v Placebo

Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	WOMAC Physical Function, LEVI-04, 2mg/kg
Statistical analysis description:	
WOMAC physical function, least squares mean difference change from baseline versus placebo	
Comparison groups	LEVI-04 2.0 mg/kg v Placebo
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	-0.46
Variability estimate	Standard error of the mean
Dispersion value	0.22

Secondary: WOMAC Stiffness	
End point title	WOMAC Stiffness
End point description:	
Least Squares Mean Change from Baseline in Standardized WOMAC Stiffness Subscale Score versus placebo	
End point type	Secondary
End point timeframe:	
Baseline to week 17 versus placebo	

End point values	LEVI-04 0.3mg/kg	LEVI-04 1.0mg/kg	LEVI-04 2.0 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	119	116	113
Units: Subjects	118	119	116	113

Statistical analyses

Statistical analysis title	WOMAC Stiffness LEVI-04 0.3mg/kg
Statistical analysis description: LSM Difference Mean Change from Baseline in Standardized WOMAC Stiffness Subscale versus placebo	
Comparison groups	Placebo v LEVI-04 0.3mg/kg
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	-0.35
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	WOMAC Stiffness LEVI-04 1mg/kg
Statistical analysis description: Mean Change from Baseline in Standardized WOMAC Stiffness Subscale Score versus placebo	
Comparison groups	LEVI-04 1.0mg/kg v Placebo
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.56
upper limit	-0.57
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	WOMAC Stiffness LEVI-04 2mg/kg
Statistical analysis description:	
LSM Difference Mean Change from Baseline in Standardized WOMAC Stiffness Subscale Score versus placebo	
Comparison groups	LEVI-04 2.0 mg/kg v Placebo
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.95
upper limit	-0.95
Variability estimate	Standard error of the mean
Dispersion value	0.25

Secondary: Post-Staircase Evoked Pain Procedure (StEPP) Pain Intensity	
End point title	Post-Staircase Evoked Pain Procedure (StEPP) Pain Intensity
End point description:	
LSM Difference Change from Baseline in Post-Staircase Evoked Pain Procedure (StEPP) Pain Intensity versus placebo	
End point type	Secondary
End point timeframe:	
Baseline to Week 17	

End point values	LEVI-04 0.3mg/kg	LEVI-04 1.0mg/kg	LEVI-04 2.0 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	119	113	110
Units: Subjects	111	119	113	110

Statistical analyses

Statistical analysis title	StEPP Change from Baseline LEVI 04 0.3mg/kg
Statistical analysis description:	
LSM Difference Change from Baseline in Post-Staircase Evoked Pain Procedure (StEPP) Pain Intensity versus placebo	

Comparison groups	LEVI-04 0.3mg/kg v Placebo
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Median difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.28

Statistical analysis title	StEPP Change from Baseline LEVI 04 1mg/kg

Statistical analysis description:

LSM Difference Mean Change from Baseline in Post-Staircase Evoked Pain Procedure (StEPP) Pain Intensity versus placebo

Comparison groups	LEVI-04 1.0mg/kg v Placebo
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	-0.31
Variability estimate	Standard error of the mean
Dispersion value	0.28

Statistical analysis title	StEPP Change from Baseline LEVI-04 2mg/kg

Statistical analysis description:

LSM Difference Mean Change from Baseline in Post-Staircase Evoked Pain Procedure (StEPP) Pain Intensity versus placebo

Comparison groups	LEVI-04 2.0 mg/kg v Placebo

Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.76
upper limit	-0.66
Variability estimate	Standard error of the mean
Dispersion value	0.28

Secondary: Patient Global Assessment (PGA)

End point title	Patient Global Assessment (PGA)
End point description:	
LSM Difference Mean Change from Baseline in Patient Global Assessment (PGA) versus placebo	
End point type	Secondary
End point timeframe:	
Baseline to Week 17	

End point values	LEVI-04 0.3mg/kg	LEVI-04 1.0mg/kg	LEVI-04 2.0 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	119	116	113
Units: Subjects	118	119	116	113

Statistical analyses

Statistical analysis title	PGA Change from Baseline LEVI-04, 0.3mg/kg
Statistical analysis description:	
LSM Difference Change from Baseline in Patient Global Assessment (PGA)	
Comparison groups	LEVI-04 0.3mg/kg v Placebo
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.13
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.26

Statistical analysis title	PGA Change from Baseline LEVI-04, 1mg/kg
Statistical analysis description:	
Mean Change from Baseline in Patient Global Assessment (PGA)	
Comparison groups	LEVI-04 1.0mg/kg v Placebo
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.44
upper limit	-0.42
Variability estimate	Standard error of the mean
Dispersion value	0.26

Statistical analysis title	PGA Change from Baseline LEVI-04, 2mg/kg
Statistical analysis description:	
LSM Difference Change from Baseline in Patient Global Assessment (PGA) versus placebo	
Comparison groups	LEVI-04 2.0 mg/kg v Placebo
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Median difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.59
upper limit	-0.56
Variability estimate	Standard error of the mean
Dispersion value	0.26

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of signing the informed consent until the end of the study (week 30)

Adverse event reporting additional description:

Adverse events were reported by participants, or via laboratory findings (blood, urine, ECG, vital signs) and imaging (X-rays of all large joints at baseline and week 20 and MRI of both knees at baseline and the target knee at week 20).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	LEVI-04 0.3mg/kg

Reporting group description:

LEVI-04 0.3 mg/kg intravenous infusion

Reporting group title	LEVI-04 1.0mg/kg

Reporting group description:

LEVI-04 1.0 mg/kg intravenous infusion

Reporting group title	LEVI-04 2.0 mg/kg

Reporting group description:

LEVI-04 2.0 mg/kg intravenous infusion

Reporting group title	Placebo

Reporting group description:

Placebo comparator (saline vehicle)

Serious adverse events	LEVI-04 0.3mg/kg	LEVI-04 1.0mg/kg	LEVI-04 2.0 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	3 / 129 (2.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tongue cancer metastatic			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (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

Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (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
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (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	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 129 (2.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tongue cancer metastatic			
subjects affected / exposed	0 / 129 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 129 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 129 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 129 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rotator cuff syndrome			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	LEVI-04 0.3mg/kg	LEVI-04 1.0mg/kg	LEVI-04 2.0 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 129 (27.91%)	36 / 130 (27.69%)	58 / 129 (44.96%)

Nervous system disorders			
Headache			
subjects affected / exposed	4 / 129 (3.10%)	3 / 130 (2.31%)	8 / 129 (6.20%)
occurrences (all)	7	3	11
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 129 (8.53%)	15 / 130 (11.54%)	15 / 129 (11.63%)
occurrences (all)	15	19	19
Back pain			
subjects affected / exposed	3 / 129 (2.33%)	5 / 130 (3.85%)	8 / 129 (6.20%)
occurrences (all)	3	5	9
Pain in extremity			
subjects affected / exposed	3 / 129 (2.33%)	7 / 130 (5.38%)	5 / 129 (3.88%)
occurrences (all)	3	9	5
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 129 (4.65%)	8 / 130 (6.15%)	13 / 129 (10.08%)
occurrences (all)	7	8	14
Upper respiratory tract infection			
subjects affected / exposed	4 / 129 (3.10%)	4 / 130 (3.08%)	5 / 129 (3.88%)
occurrences (all)	4	4	6
COVID-19			
subjects affected / exposed	5 / 129 (3.88%)	2 / 130 (1.54%)	4 / 129 (3.10%)
occurrences (all)	5	2	4

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 129 (48.06%)		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 129 (4.65%)		
occurrences (all)	12		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	20 / 129 (15.50%)		
occurrences (all)	24		
Back pain			

subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	3 / 129 (2.33%) 3 5 / 129 (3.88%) 5		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all)	 13 / 129 (10.08%) 14 7 / 129 (5.43%) 7 8 / 129 (6.20%) 9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported