



Clinical trial results:

Proof of efficacy, maintenance of efficacy, long-term safety and investigation of the potential for dependence and abuse and the effect of abrupt drug withdrawal of VER-01 in a multicenter study in the treatment of patients with chronic non-specific low back pain

Summary

EudraCT number	2020-000107-36
Trial protocol	DE AT
Global end of trial date	26 March 2024

Results information

Result version number	v1 (current)
This version publication date	10 May 2026
First version publication date	10 May 2026

Trial information

Trial identification

Sponsor protocol code	VER-CLBP-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04940741
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertanical GmbH
Sponsor organisation address	Am Haag 14, Gräfelting, Germany, 82166
Public contact	Dr Janin Grajcarek, Vertanical GmbH, +49 89 7879790-78, regulatory@vertanical.com
Scientific contact	Dr Janin Grajcarek, Vertanical GmbH, +49 89 7879790-78, regulatory@vertanical.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	26 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2024
Global end of trial reached?	Yes
Global end of trial date	26 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Phase A was to demonstrate the efficacy of VER 01 in terms of pain reduction compared to placebo in the treatment of patients with chronic non-specific low back pain (CLBP) when drug treatment is indicated and a previous optimised treatment with non-opioids has not led to sufficient pain relief or was unsuitable due to contraindications or intolerance.

The primary objective of Phase B was to investigate the long-term safety and the potential for dependence and abuse of VER-01 over 26 weeks.

The primary objective of Phase C was to investigate the long-term safety, the potential for dependence and abuse and the effects of sudden drug withdrawal for long-term open-label treatment with VER-01 over an additional 26 weeks.

The primary objective of Phase D was to demonstrate the maintenance of efficacy of VER-01 in terms of pain reduction on a placebo-controlled basis.

Protection of trial subjects:

The study has been conducted in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy:

Ibuprofen (tablets, dose strength 800 mg) was available as rescue medication. It could be taken at a daily dose of up to 2,400 mg and, independent of dose, on a maximum of 3 days per week. No intake was allowed during 24 hours prior to visits, except for the follow-up visit and unscheduled visits. If ibuprofen was contraindicated paracetamol could be used as a rescue medication in the form of tablets (500 mg) at a maximum daily dose of 4,000 mg and, independent of dose, on a maximum of 3 days a week. No intake was allowed during 24 hours prior to visits, except for the follow-up visit and unscheduled visits.

Evidence for comparator: -

Actual start date of recruitment	07 July 2021
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	Austria: 85
Country: Number of subjects enrolled	Germany: 735
Worldwide total number of subjects	820
EEA total number of subjects	820

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)	658
From 65 to 84 years	162
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Phase A: 820 randomized/included; 815 treated

Phase B: 525 randomized/included; 524 treated

Phase C: 155 randomized/included; 154 treated

Phase D: 116 randomized/included; 116 treated

Phases C and D ran in parallel. Patients who completed Phase B could be assigned to one of these 2 phases (could not be replicated exactly in EudraCT form).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase A VER-01

Arm description:

After Screening and a 1-week run-in phase to determine the baseline pain score, patients were to be randomised to a 3-week double-blind self-titration with VER-01 for individual dose finding.

Subsequently, patients were to be treated with the patient-specific optimal daily dose identified during the titration phase for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	VER-01
Investigational medicinal product code	
Other name	Standardised cannabis extract (containing 21 mg THC per gram drug product)
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

During the 3-week self-titration phase for individual dose finding, patients were to be treated up to twice daily with increasing doses according to the titration schedule until the patient-specific optimal daily dose up to the maximum allowed daily dose of 32.5 mg THC was reached based on efficacy (symptom relief) and safety (side effects). Patients were then to be treated with the patient-specific optimal daily dose for 12 weeks. The daily dose determined in the titration phase could be adjusted upwards or downwards if their condition or concomitant medication changed or to manage side effects.

Arm title	Phase A Placebo
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Arm description:

After Screening and a 1-week run-in phase to determine the baseline pain score, patients were to be randomised to a 3-week double-blind self-titration with Placebo for individual dose finding.

Subsequently, patients were to be treated with the patient-specific optimal daily dose identified during the titration phase for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Standardised cannabis extract with max. 0.1 mg/g THC
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

During the 3-week self-titration phase for individual dose finding, patients were to be treated up to twice daily with increasing doses according to the titration schedule until the patient-specific optimal daily dose up to the maximum allowed daily dose of 32.5 mg THC was reached based on efficacy (symptom relief) and safety (side effects). Patients were then to be treated with the patient-specific optimal daily dose for 12 weeks. The daily dose determined in the titration phase could be adjusted upwards or downwards if their condition or concomitant medication changed or to manage side effects.

Number of subjects in period 1	Phase A VER-01	Phase A Placebo
Started	394	426
Completed	267	359
Not completed	127	67
Consent withdrawn by subject	17	9
Physician decision	6	5
Adverse event, non-fatal	68	15
Other	9	9
Non-compliance with study drug	3	3
Lost to follow-up	6	7
Not treated	4	1
Lack of efficacy	14	18

Period 2

Period 2 title	Phase B
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Phase B VER-01
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Arm description:

After 3 weeks of open-label self-titration with VER 01, patients took VER-01 at their individual optimal dose over a period of 6 months (26 weeks).

Arm type	Experimental
Investigational medicinal product name	VER-01
Investigational medicinal product code	
Other name	Standardised cannabis extract (containing 21 mg THC per gram drug product)
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

After 3 weeks of open-label self-titration with VER-01, the patients took VER-01 at their individual optimal dose over a period of 6 months (26 weeks). The daily dose could be adjusted downwards or upwards as required, up to the maximum allowed daily dose of 32.5 mg THC. In Phase B, 4 regular

visits (B7, B8, B9, B10) and 4 visits for the return and dispensing of the IMP (AID1, AID2, AID3, AID4) took place.

Number of subjects in period 2^[1]	Phase B VER-01
Started	525
Completed	342
Not completed	183
Consent withdrawn by subject	26
Physician decision	10
Adverse event, non-fatal	76
Other	18
Pregnancy	1
Non-compliance with study drug	3
Lost to follow-up	13
Lack of efficacy	36

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Patients who completed Phase A could be enrolled in Phase B, which had a target number of 500 patients. After 3 weeks of open-label self-titration with VER-01, patients took VER-01 at their individual optimal dose over a period of 6 months (26 weeks). (The exact design could not be fully mirrored in the EudraCT form.)

Period 3

Period 3 title	Phase C
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Phase C VER-01
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Arm description:

Patients took VER-01 for an additional 26 weeks, after which intake was abruptly stopped and a 2-week wash-out phase was entered.

Arm type	Experimental
Investigational medicinal product name	VER-01
Investigational medicinal product code	
Other name	Standardised cannabis extract (containing 21 mg THC per gram drug product)
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Patients who completed Phase B and did not violate any of the inclusion or exclusion criteria for Phase C could be assigned to Phase C. Patients continued taking VER-01 for a further 26 weeks, followed by a 2-week wash-out phase. A total of 4 regular visits (C11, C12, C13, C14) and 4 visits for withdrawal and dispensing of the IMP (AID5, AID6, AID7, AID8) took place.

Number of subjects in period 3^[2]	Phase C VER-01
Started	155
Completed	135
Not completed	20
Consent withdrawn by subject	5
Adverse event, non-fatal	5
Other	7
Pregnancy	1
Not treated	1
Lack of efficacy	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Phases C and D ran in parallel. Phase B patients were statistically assigned to ensure Phase D included ≥ 80 (target: 120) responders ($\geq 30\%$ pain reduction in Phase B). Once recruitment targets for C and D were met, subsequent patients completed the study after Phase B. (The exact design could not be fully mirrored in the EudraCT form.)

Period 4

Period 4 title	Phase D
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase D VER-01

Arm description:

After randomisation at the beginning of the phase, patients were to receive 4 weeks of treatment with VER-01. All patients were then to be followed-up in a 2-week wash-out phase.

Arm type	Experimental
Investigational medicinal product name	VER-01
Investigational medicinal product code	
Other name	Standardised cannabis extract (containing 21 mg THC per gram drug product)
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Patients who completed Phase B and did not violate any of the inclusion or exclusion criteria for Phase D could be assigned to Phase D. After randomisation (Randomisation 2) at the beginning of the phase, patients were to receive 4 weeks of treatment.

Arm title	Phase D Placebo
Arm description: After randomisation at the beginning of the phase, patients were to receive 4 weeks of treatment with Placebo (sudden, blinded drug withdrawal). All patients were then to be followed-up in a 2-week wash-out phase.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Standardised cannabis extract with max. 0.1 mg/g THC
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Patients who completed Phase B and did not violate any of the inclusion or exclusion criteria for Phase D could be assigned to Phase D. After randomisation (Randomisation 2) at the beginning of the phase, patients were to receive 4 weeks of treatment. Patients who received placebo in this phase were to undergo sudden, blinded drug withdrawal. This was to be followed by a 2-week wash-out phase for follow-up for all patients.

Number of subjects in period 4^[3]	Phase D VER-01	Phase D Placebo
Started	52	64
Completed	52	57
Not completed	0	7
Consent withdrawn by subject	-	1
Physician decision	-	1
Adverse event, non-fatal	-	1
Other	-	2
Lost to follow-up	-	1
Lack of efficacy	-	1

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Phases C and D ran in parallel. Phase B patients were statistically assigned to ensure Phase D included ≥ 80 (target: 120) responders ($\geq 30\%$ pain reduction in Phase B). Once recruitment targets for C and D were met, subsequent patients completed the study after Phase B. (The exact design could not be fully mirrored in the EudraCT form.)

Baseline characteristics

Reporting groups

Reporting group title	Phase A
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Reporting group description: -

Reporting group values	Phase A	Total	
Number of subjects	820	820	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	658	658	
From 65-84 years	162	162	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	52.2		
standard deviation	± 13.8	-	
Gender categorical			
Number of female and male patients is corresponding to the total number of treated patients.			
Units: Subjects			
Female	461	461	
Male	359	359	

End points

End points reporting groups

Reporting group title	Phase A VER-01
Reporting group description: After Screening and a 1-week run-in phase to determine the baseline pain score, patients were to be randomised to a 3-week double-blind self-titration with VER-01 for individual dose finding. Subsequently, patients were to be treated with the patient-specific optimal daily dose identified during the titration phase for 12 weeks.	
Reporting group title	Phase A Placebo
Reporting group description: After Screening and a 1-week run-in phase to determine the baseline pain score, patients were to be randomised to a 3-week double-blind self-titration with Placebo for individual dose finding. Subsequently, patients were to be treated with the patient-specific optimal daily dose identified during the titration phase for 12 weeks.	
Reporting group title	Phase B VER-01
Reporting group description: After 3 weeks of open-label self-titration with VER 01, patients took VER-01 at their individual optimal dose over a period of 6 months (26 weeks).	
Reporting group title	Phase C VER-01
Reporting group description: Patients took VER-01 for an additional 26 weeks, after which intake was abruptly stopped and a 2-week wash-out phase was entered.	
Reporting group title	Phase D VER-01
Reporting group description: After randomisation at the beginning of the phase, patients were to receive 4 weeks of treatment with VER-01. All patients were then to be followed-up in a 2-week wash-out phase.	
Reporting group title	Phase D Placebo
Reporting group description: After randomisation at the beginning of the phase, patients were to receive 4 weeks of treatment with Placebo (sudden, blinded drug withdrawal). All patients were then to be followed-up in a 2-week wash-out phase.	

Primary: Change from baseline in mean pain intensity measured in the morning on an 11-point Numeric Rating Scale (NRS) (Phase A)

End point title	Change from baseline in mean pain intensity measured in the morning on an 11-point Numeric Rating Scale (NRS) (Phase A)
End point description: Mean value of Week 15 compared to the mean value of the 7 days prior to Visit A2 [Week -1] with daily documentation of pain intensity in the eDiary by the patient.	
End point type	Primary
End point timeframe: Baseline to Week 15	

End point values	Phase A VER-01	Phase A Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	390	425		
Units: Points				
least squares mean (standard error)	-1.9 (\pm 0.2)	-1.4 (\pm 0.2)		

Statistical analyses

Statistical analysis title	All patients
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.3

Primary: Time to treatment failure defined as the time in days from randomisation to Phase D until the first day of treatment failure

End point title	Time to treatment failure defined as the time in days from randomisation to Phase D until the first day of treatment failure
End point description:	Treatment failure was assessed by the daily calculated seven-day mean value of the NRS pain score in the morning during the treatment phase of Phase D, which must have deteriorated by at least 20% and at least 1 point compared to baseline (mean value of Week 43).
End point type	Primary
End point timeframe:	
Baseline to Week 4	

End point values	Phase D VER-01	Phase D Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	63		
Units: Days	22	11		

Statistical analyses

Statistical analysis title	Maintenance of efficacy
Comparison groups	Phase D VER-01 v Phase D Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.288
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.27

Secondary: Change from baseline in mean pain intensity measured in the morning on an 11-point Numeric Rating Scale (NRS) (Phase A - Severe pain)

End point title	Change from baseline in mean pain intensity measured in the morning on an 11-point Numeric Rating Scale (NRS) (Phase A - Severe pain)
End point description:	
Mean value of Week 15 compared to the mean value of the 7 days prior to Visit A2 [Week -1] with daily documentation of pain intensity in the eDiary by the patient; baseline pain intensity ≥ 7 points.	
End point type	Secondary
End point timeframe:	
Baseline to Week 15	

End point values	Phase A VER-01	Phase A Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	93		
Units: Points				
arithmetic mean (standard deviation)	-3.0 (\pm 2.5)	-1.9 (\pm 2.4)		

Statistical analyses

Statistical analysis title	Patients with severe pain
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	194
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	= 0.011
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-0.1

Secondary: Change from baseline on an 11-point NRS measured in the morning for patients with a neuropathic pain component (Phase A)

End point title	Change from baseline on an 11-point NRS measured in the morning for patients with a neuropathic pain component (Phase A)
End point description: For those patients where a neuropathic pain component is very likely (> 90%); as detected by the painDETECT is a validated screening questionnaire (final score of > 18 points).	
End point type	Secondary
End point timeframe: Baseline to Week 15	

End point values	Phase A VER-01	Phase A Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	91		
Units: Points				
arithmetic mean (standard deviation)	-2.7 (± 1.9)	-1.2 (± 1.9)		

Statistical analyses

Statistical analysis title	All patients with a neuropathic pain component
Comparison groups	Phase A Placebo v Phase A VER-01
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.9

Secondary: Change from baseline in the Neuropathic Pain Symptom Inventory

(NPSI) total score in patients with a painDETECT final score >18 (Phases A and B)

End point title	Change from baseline in the Neuropathic Pain Symptom Inventory (NPSI) total score in patients with a painDETECT final score >18 (Phases A and B)
End point description: The NPSI is scored as the sum of 10 pain descriptor items, each rated on a scale from 0 to 10, with 10 representing the strongest attestation to that descriptor. Thus, the NPS total score ranges from 0 to 100 with 100 representing the highest degree of neuropathic-like symptoms.	
End point type	Secondary
End point timeframe: Phase A: Baseline to Week 15 Phase B: Baseline to Week 44	

End point values	Phase A VER-01	Phase A Placebo	Phase B VER-01	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	91	115 ^[1]	
Units: Points				
least squares mean (standard error)	-14.4 (± 3.3)	-7.2 (± 2.8)	-21.2 (± 19.1)	

Notes:

[1] - For Phase B: arithmetic mean (standard deviation)

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.017
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	-1.3

Secondary: NPSI subscores absolute change from baseline for patients with neuropathic pain (Phase A)

End point title	NPSI subscores absolute change from baseline for patients with neuropathic pain (Phase A)
End point description: The NPSI is scored as the sum of 10 pain descriptor items, each rated on a scale from 0 to 10, with 10 representing the strongest attestation to that descriptor. Thus, the NPS total score ranges from 0 to 100 with 100 representing the highest degree of neuropathic-like symptoms.	
End point type	Secondary

End point timeframe:

Baseline to Week 15

End point values	Phase A VER-01	Phase A Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	91		
Units: Points				
arithmetic mean (standard deviation)				
Superficial spontaneous pain	-2.3 (± 2.9)	-0.9 (± 3.2)		
Deep spontaneous pain	-2.1 (± 2.7)	-0.9 (± 2.7)		
Evoked pain	-1.5 (± 2.3)	-0.3 (± 2.1)		
Abnormal sensations	-2.3 (± 2.7)	-1.0 (± 2.6)		

Statistical analyses

Statistical analysis title	Superficial spontaneous pain
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.015
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.3

Statistical analysis title	Deep spontaneous pain
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.3

Statistical analysis title	Evoked pain
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.003
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	-0.4

Statistical analysis title	Abnormal sensations
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.006
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.4

Secondary: Change from baseline in mean pain intensity measured in the morning on an 11-point NRS (Phase B and D)

End point title	Change from baseline in mean pain intensity measured in the morning on an 11-point NRS (Phase B and D)
End point description:	
Mean value of the end of treatment compared to the mean value prior treatment with daily documentation of pain intensity in the eDiary by the patient.	
End point type	Secondary

End point timeframe:

Phase B: Baseline to Week 44

Phase D: Week 44 to 50

End point values	Phase B VER-01	Phase D VER-01	Phase D Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	524	51	63	
Units: Points				
arithmetic mean (standard deviation)	-2.9 (± 2.1)	0.5 (± 1.1)	1.0 (± 1.3)	

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase D VER-01 v Phase D Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.034
Method	t-test, 2-sided

Secondary: Percentage of Pain Responders (Phases A and B)

End point title	Percentage of Pain Responders (Phases A and B)
End point description: Patient was defined as a 30% / 50% pain responder if the relative improvement over baseline (Week -1) in mean pain intensity in the morning on the 11-point NRS at Week 15 / Week 44 was at least 30% / 50%. For ≥2-point pain reduction: 46.9% for VER-01 vs 35.6% for placebo (p = 0.001)	
End point type	Secondary
End point timeframe: Phase A: Baseline to Week 15 Phase B: Baseline to Week 44	

End point values	Phase A VER-01	Phase A Placebo	Phase B VER-01	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	425	524	
Units: %				
number (not applicable)				
30% pain reduction	54.1	39.5	73.9	
50% pain reduction	32.2	22.8	51.8	

Statistical analyses

Statistical analysis title	30% pain responders
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.22
upper limit	2.26

Statistical analysis title	50% pain responders
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.01
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	2.22

Statistical analysis title	Number needed to treat to benefit (NNTB)
Comparison groups	Phase A VER-01 v Phase A Placebo

Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Chi-squared
Parameter estimate	NNTB
Point estimate	6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.42
upper limit	15.05

Secondary: Cumulative dose of rescue medication - Ibuprofen tablets (Phase A)

End point title	Cumulative dose of rescue medication - Ibuprofen tablets (Phase A)
End point description:	
The use of rescue medication was only permitted in the case of acute pain worsening.	
End point type	Secondary
End point timeframe:	
Baseline to Week 15	

End point values	Phase A VER-01	Phase A Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	390	425		
Units: Tablets				
arithmetic mean (standard deviation)	10.5 (± 14.2)	18.3 (± 53.8)		

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: Cumulative dose of rescue medication - Ibuprofen in g (Phase A)

End point title	Cumulative dose of rescue medication - Ibuprofen in g (Phase A)
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End point description:

The use of rescue medication was only permitted in the case of acute pain worsening.

End point type	Secondary
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End point timeframe:

Baseline to Week 15

End point values	Phase A VER-01	Phase A Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	390	425		
Units: Gram (g)				
arithmetic mean (standard deviation)	8.4 (± 11.4)	14.6 (± 43.1)		

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: Change from baseline in mean NRS sleep quality (Phases A and B)

End point title	Change from baseline in mean NRS sleep quality (Phases A and B)
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End point description:

NRS Sleep Quality is a single-item measure that instructs the patient to select the number that best describes the quality of your sleep during the past 24 hours, where 0 is best possible sleep and 10 is worst possible sleep.

End point type	Secondary
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End point timeframe:

Phase A: Baseline to Week 15

Phase B: Baseline to Week 44

End point values	Phase A VER-01	Phase A Placebo	Phase B VER-01	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	425	524	
Units: Points				
arithmetic mean (standard deviation)	-2.2 (± 2.2)	-1.5 (± 2.0)	-2.9 (± 2.1)	

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.3

Secondary: Change in Medical Outcomes Study Sleep Scale (MOS-SS) subscore from baseline (Phase A)

End point title	Change in Medical Outcomes Study Sleep Scale (MOS-SS) subscore from baseline (Phase A)
End point description: MOS-SS (revised version of 2010) includes 12 questions to assess sleep quality. Sleep quality over the past 4 weeks was assessed. The evaluation of the MOS-SS was based on 2 sleep problems indices and 6 scale scores (sleep disturbance, sleep adequacy, somnolence, snoring, shortness of breath and headache, sleep quantity), and on the dichotomous optimal sleep scale ('optimal' vs. 'not optimal').	
End point type	Secondary
End point timeframe: Baseline to Week 15	

End point values	Phase A VER-01	Phase A Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	390	425		
Units: Points				
arithmetic mean (standard deviation)				
Sleep problems index I	6.5 (± 9.1)	4.1 (± 8.8)		
Sleep problems index II	6.8 (± 8.9)	4.5 (± 8.3)		

Statistical analyses

Statistical analysis title	Sleep problems index I
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	t-test, 2-sided

Statistical analysis title	Sleep problems Index II
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.001
Method	t-test, 2-sided

Secondary: Change from baseline in Roland Morris Disability Questionnaire (RMDQ) total score (Phase A)

End point title	Change from baseline in Roland Morris Disability Questionnaire (RMDQ) total score (Phase A)
End point description:	The RMD Questionnaire consists of 24 questions on bodily function and disability due to low back pain. The patient-individual total score was calculated as the sum of the scores and ranged from 0 (no disability) to 24 (severe disability).
End point type	Secondary
End point timeframe:	Baseline to Week 15

End point values	Phase A VER-01	Phase A Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	390	425		
Units: Points				
arithmetic mean (standard deviation)	-3.1 (± 4.0)	-2.0 (± 4.1)		

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase A VER-01 v Phase A Placebo

Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-1.1

Secondary: Percentage of 30% RMDQ responders (Phase A)

End point title	Percentage of 30% RMDQ responders (Phase A)
End point description:	
The RMD Questionnaire consists of 24 questions on bodily function and disability due to low back pain. The patient-individual total score was calculated as the sum of the scores and ranged from 0 (no disability) to 24 (severe disability).	
End point type	Secondary
End point timeframe:	
Baseline to Week 15	

End point values	Phase A VER-01	Phase A Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	390	425		
Units: %				
number (not applicable)	51.7	42.2		

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	2.01

Secondary: Percentage of patients with improvement of symptoms (Patient Global Impression of Change [PGIC]) (Phases A and B)

End point title	Percentage of patients with improvement of symptoms (Patient Global Impression of Change [PGIC]) (Phases A and B)
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End point description:

The global impression of change (PGIC) by the patient was assessed at the end of the treatment phase at using the PGIC with the following question: 'How is your low back pain in comparison to before participation in the study?'. The responses were recorded numerically on a 7-point Likert scale. The scale ranged from 0 (very much better) to 6 (very much worse). The assessment was dichotomised to 'improvement of symptoms' (assessment of 0 or 1) or 'no improvement of symptoms' (assessment of 2, 3 or 4).

Improvement of symptoms = very much better and much better.

End point type	Secondary
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End point timeframe:

Phase A: Baseline to Week 15

Phase B: Baseline to Week 44

End point values	Phase A VER-01	Phase A Placebo	Phase B VER-01	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	425	524	
Units: %				
number (not applicable)	45.1	23.4	60.4	

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Number needed to treat to benefit (NNTB)
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.43
upper limit	6.99

Secondary: Change from baseline of SF-36v2 health questionnaire for physical components (Phases A and B)

End point title	Change from baseline of SF-36v2 health questionnaire for physical components (Phases A and B)
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End point description:

The Short Form 36v2 (SF-36v2) health questionnaire contains 36 questions about physical and mental wellbeing. The SF-36v2 was evaluated based on 8 domain scores (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health). The physical components were summarised to form the Physical Health Component Summary [PCS].

The scores range from 0 (maximum disability) to 100 (no disability).

End point type	Secondary
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End point timeframe:

Phase A: Baseline to Week 15

Phase B: Baseline to Week 44

End point values	Phase A VER-01	Phase A Placebo	Phase B VER-01	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	425	524	
Units: Points				
arithmetic mean (standard deviation)	5.9 (± 6.8)	3.7 (± 7.0)	13.4 (± 18.7)	

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	3.2

Secondary: Percentage of patients with improvement in quality of life (SF-36v2) (Phases A and B)

End point title	Percentage of patients with improvement in quality of life (SF-36v2) (Phases A and B)
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End point description:

Improvement in quality of life = somewhat better now than 1 year ago, much better now than 1 year ago.

End point type	Secondary
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End point timeframe:

Phase A: Baseline to Week 15

Phase B: Baseline to Week 44

End point values	Phase A VER-01	Phase A Placebo	Phase B VER-01	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	425	524	
Units: %				
number (not applicable)	46.1	31.2	65.6	

Statistical analyses

Statistical analysis title	VER-01 vs Placebo
Comparison groups	Phase A VER-01 v Phase A Placebo
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events have been recorded continuously from the first test product intake until the end of the study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Phase A VER-01
Reporting group description: -	
Reporting group title	Phase A Placebo
Reporting group description: -	
Reporting group title	Phase B VER-01
Reporting group description: -	
Reporting group title	Phase C VER-01
Reporting group description: -	
Reporting group title	Phase D VER-01
Reporting group description: -	
Reporting group title	Phase D Placebo
Reporting group description: -	

Serious adverse events	Phase A VER-01	Phase A Placebo	Phase B VER-01
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 390 (6.15%)	29 / 425 (6.82%)	21 / 524 (4.01%)
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)			
Renal cell carcinoma			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Small intestine carcinoma metastatic			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Adenocarcinoma of colon			

subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 390 (0.26%)	2 / 425 (0.47%)	2 / 524 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic venous thrombosis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Peripheral artery occlusion			

subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Capsular contracture associated with breast implant			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stenosis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	2 / 524 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Erectile dysfunction			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Burnout syndrome			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	0 / 524 (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
Hallucination			

subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	2 / 524 (0.38%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, auditory			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed mood			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, visual			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritability			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	2 / 524 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic specific antigen increased			

subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Tendon injury			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Tendon rupture			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Wound			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Fall			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			

subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Syringomyelia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 390 (0.26%)	1 / 425 (0.24%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Coronary artery disease			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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

Mitral valve incompetence			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Aortic valve incompetence			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular disorder			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	3 / 390 (0.77%)	0 / 425 (0.00%)	3 / 524 (0.57%)
occurrences causally related to treatment / all	3 / 4	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	3 / 524 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydromyelia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Headache			

subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	2 / 524 (0.38%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Sciatica			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Dizziness			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	2 / 524 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dural arteriovenous fistula			

subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukoencephalopathy			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic intolerance			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral artery occlusion			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Retinal tear			
subjects affected / exposed	1 / 390 (0.26%)	2 / 425 (0.47%)	0 / 524 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	0 / 524 (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
Retinal detachment			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Ocular hypertension			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Vitreous detachment			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Corneal perforation			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vision blurred			

subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis microscopic			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Haematochezia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Abdominal pain upper			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal discomfort			

subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	0 / 524 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Autoimmune thyroiditis			

subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	2 / 524 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	3 / 524 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	0 / 524 (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
Back pain			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Bursitis			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical spinal stenosis			

subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Muscle tightness			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exostosis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	1 / 390 (0.26%)	1 / 425 (0.24%)	0 / 524 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 390 (0.26%)	1 / 425 (0.24%)	0 / 524 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess jaw			

subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Omphalitis			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Urinary tract infection			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	2 / 524 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	1 / 524 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			

subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	0 / 524 (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
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 390 (0.00%)	0 / 425 (0.00%)	0 / 524 (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
Decreased appetite			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 390 (0.26%)	0 / 425 (0.00%)	0 / 524 (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
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 390 (0.00%)	1 / 425 (0.24%)	0 / 524 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase C VER-01	Phase D VER-01	Phase D Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 154 (11.69%)	1 / 52 (1.92%)	1 / 64 (1.56%)
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)			
Renal cell carcinoma			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Small intestine carcinoma metastatic			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Adenocarcinoma of colon			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Breast cancer			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Prostate cancer			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Pelvic venous thrombosis			

subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Lymphoedema			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Peripheral artery occlusion			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Hypotension			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Capsular contracture associated with breast implant			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Gait disturbance			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Pain			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Stenosis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Erectile dysfunction			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Ovarian cyst			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Pulmonary embolism			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Psychiatric disorders			
Burnout syndrome			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Hallucination, auditory			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Depressed mood			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Hallucination, visual			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Irritability			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Suicidal ideation			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Product issues			

Device dislocation			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic specific antigen increased			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Weight decreased			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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			
Ankle fracture			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Hand fracture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Tendon injury			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Tendon rupture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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

Wound			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Fall			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Head injury			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Congenital, familial and genetic disorders			
Syringomyelia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Angina pectoris			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Arrhythmia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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

Bradycardia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Coronary artery disease			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Mitral valve incompetence			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Myocardial infarction			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Aortic valve incompetence			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Cardiovascular disorder			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Myocarditis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	2 / 154 (1.30%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Hydromyelia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Headache			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Polyneuropathy			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Sciatica			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Dizziness			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Aphasia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Cerebral haemorrhage			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Dural arteriovenous fistula			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Hemiparesis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Leukoencephalopathy			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Monoparesis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Orthostatic intolerance			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Vertebral artery occlusion			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Blood and lymphatic system disorders			
Thrombocytopenia			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Eye disorders			
Retinal tear			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Cataract			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Retinal detachment			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Conjunctival haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Ocular hypertension			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Vitreous detachment			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Corneal perforation			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Uveitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Vision blurred			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	2 / 154 (1.30%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis microscopic			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Haematochezia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Abdominal pain upper			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Intestinal haemorrhage			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Melaena			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Abdominal discomfort			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Cholelithiasis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Skin ulcer			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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

Acute kidney injury			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Hypothyroidism			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Osteoarthritis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Osteochondrosis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Spinal stenosis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 52 (1.92%)	0 / 64 (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
Back pain			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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

Bursitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Cervical spinal stenosis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Muscle tightness			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Exostosis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Synovitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Infections and infestations			
Diverticulitis			
subjects affected / exposed	2 / 154 (1.30%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Pneumonia			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Abscess jaw			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Omphalitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Vestibular neuronitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Urinary tract infection			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Febrile infection			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Gastroenteritis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Sepsis			

subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 52 (0.00%)	0 / 64 (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
Decreased appetite			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Diabetes mellitus			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 154 (0.00%)	0 / 52 (0.00%)	0 / 64 (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

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

Non-serious adverse events	Phase A VER-01	Phase A Placebo	Phase B VER-01
Total subjects affected by non-serious adverse events subjects affected / exposed	325 / 390 (83.33%)	286 / 425 (67.29%)	403 / 524 (76.91%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	167 / 390 (42.82%)	22 / 425 (5.18%)	134 / 524 (25.57%)
occurrences (all)	263	25	190
Headache			
subjects affected / exposed	62 / 390 (15.90%)	53 / 425 (12.47%)	50 / 524 (9.54%)
occurrences (all)	81	84	84
Somnolence			
subjects affected / exposed	46 / 390 (11.79%)	3 / 425 (0.71%)	28 / 524 (5.34%)
occurrences (all)	49	3	32
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	59 / 390 (15.13%)	22 / 425 (5.18%)	34 / 524 (6.49%)
occurrences (all)	63	27	37
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	64 / 390 (16.41%)	16 / 425 (3.76%)	47 / 524 (8.97%)
occurrences (all)	86	17	68
Dry mouth			
subjects affected / exposed	51 / 390 (13.08%)	16 / 425 (3.76%)	40 / 524 (7.63%)
occurrences (all)	57	18	55
Diarrhoea			
subjects affected / exposed	32 / 390 (8.21%)	18 / 425 (4.24%)	40 / 524 (7.63%)
occurrences (all)	35	22	50
Toothache			
subjects affected / exposed	7 / 390 (1.79%)	7 / 425 (1.65%)	10 / 524 (1.91%)
occurrences (all)	7	8	11
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	6 / 390 (1.54%)	6 / 425 (1.41%)	5 / 524 (0.95%)
occurrences (all)	6	6	5
Musculoskeletal and connective tissue disorders			

Back pain subjects affected / exposed occurrences (all)	10 / 390 (2.56%) 15	16 / 425 (3.76%) 21	26 / 524 (4.96%) 33
Arthralgia subjects affected / exposed occurrences (all)	17 / 390 (4.36%) 23	20 / 425 (4.71%) 27	24 / 524 (4.58%) 33
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	43 / 390 (11.03%) 49	63 / 425 (14.82%) 73	87 / 524 (16.60%) 108
COVID-19 subjects affected / exposed occurrences (all)	43 / 390 (11.03%) 43	36 / 425 (8.47%) 36	70 / 524 (13.36%) 72
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 390 (1.03%) 4	2 / 425 (0.47%) 2	13 / 524 (2.48%) 16
Gastrointestinal infection subjects affected / exposed occurrences (all)	6 / 390 (1.54%) 6	6 / 425 (1.41%) 6	10 / 524 (1.91%) 10

Non-serious adverse events	Phase C VER-01	Phase D VER-01	Phase D Placebo
Total subjects affected by non-serious adverse events subjects affected / exposed	125 / 154 (81.17%)	13 / 52 (25.00%)	15 / 64 (23.44%)
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	39 / 154 (25.32%) 60	0 / 52 (0.00%) 0	1 / 64 (1.56%) 1
Headache subjects affected / exposed occurrences (all)	21 / 154 (13.64%) 51	3 / 52 (5.77%) 3	3 / 64 (4.69%) 6
Somnolence subjects affected / exposed occurrences (all)	7 / 154 (4.55%) 7	0 / 52 (0.00%) 0	0 / 64 (0.00%) 0
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	10 / 154 (6.49%) 13	0 / 52 (0.00%) 0	0 / 64 (0.00%) 0

Gastrointestinal disorders			
Nausea			
subjects affected / exposed	19 / 154 (12.34%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences (all)	29	0	0
Dry mouth			
subjects affected / exposed	11 / 154 (7.14%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences (all)	16	0	0
Diarrhoea			
subjects affected / exposed	16 / 154 (10.39%)	1 / 52 (1.92%)	0 / 64 (0.00%)
occurrences (all)	22	1	0
Toothache			
subjects affected / exposed	10 / 154 (6.49%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences (all)	11	0	0
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	2 / 154 (1.30%)	3 / 52 (5.77%)	1 / 64 (1.56%)
occurrences (all)	2	3	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	10 / 154 (6.49%)	1 / 52 (1.92%)	1 / 64 (1.56%)
occurrences (all)	13	1	1
Arthralgia			
subjects affected / exposed	12 / 154 (7.79%)	1 / 52 (1.92%)	1 / 64 (1.56%)
occurrences (all)	20	1	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	47 / 154 (30.52%)	2 / 52 (3.85%)	7 / 64 (10.94%)
occurrences (all)	80	2	7
COVID-19			
subjects affected / exposed	41 / 154 (26.62%)	2 / 52 (3.85%)	1 / 64 (1.56%)
occurrences (all)	43	2	1
Urinary tract infection			
subjects affected / exposed	9 / 154 (5.84%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences (all)	10	0	0
Gastrointestinal infection			

subjects affected / exposed	8 / 154 (5.19%)	0 / 52 (0.00%)	0 / 64 (0.00%)
occurrences (all)	8	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 December 2022	Adjustment of the drop-out rate to 25% in Phase A and 40% in Phase B and C and resulting increase in sample size for Phase C to 170 patients Reduction of the sample size for Phase B to 500 patients at Visit B7 Addition of Paesel & Lorei GmbH & Co. KG (re-labelling) as manufacturer Adjustment of the definition of adverse event to 'An adverse event (AE) is any negative medical incident that affects a person participating in a clinical trial' instead of '[...]to whom an investigational medicinal product was administered', as Visit A1 represents the start of the study and any event is classed as an AE from this date
10 November 2023	Adjustment of the study population of the key-secondary endpoint to patients with a painDETECT score >18 Adjustment of the case number estimation for the key-secondary endpoint Addition of an explanation of the difference between the stratification according to painDETECT score cut-off value 12 and the assessment of the key-secondary endpoint according to cut-off value 18 Adjustment of the required number of cases for Phase C to a minimum of 150 Addition of the condition that patients only proceed to Phase B after Phase A if the number of cases was not fulfilled according to protocol version 06-CA

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported