



Clinical trial results:

Multicentre, randomized, open-label study to prove an additional benefit of the full-spectrum cannabis extract VER-01 over opioids in the treatment of patients with chronic non-specific low back pain.

Summary

EudraCT number	2022-001358-41
Trial protocol	DE ES CZ
Global end of trial date	18 October 2024

Results information

Result version number	v1 (current)
This version publication date	19 November 2025
First version publication date	19 November 2025

Trial information

Trial identification

Sponsor protocol code	VER-CLBP-002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05610813
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, Regulatory Affairs, +49 89 7879790-78, regulatory@vertanical.com
Scientific contact	Dr Janin Grajcarek, Regulatory Affairs, +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	18 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 October 2024
Global end of trial reached?	Yes
Global end of trial date	18 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective was to prove a reduced risk of developing constipation under treatment with VER-01 compared to an opioid therapy at the end of Treatment Phase.

Key secondary objective was to compare the efficacy of VER-01 to an opioid therapy in terms of pain reduction and reduction of low back pain interference with sleep.

Other secondary objectives were to evaluate the safety and tolerability of VER-01 compared to an opioid therapy and to compare the efficacy of VER-01 to opioid therapy in terms of pain reduction.

Protection of trial subjects:

The study was 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:

The following rescue medications could be used in the event of acute worsening of the Chronic Low Back Pain:

Ibuprofen: maximum daily dose of up to 2,400 mg

Paracetamol (when ibuprofen was contraindicated): maximum daily dose of up to 4,000 mg

Evidence for comparator:

The comparative opioid therapy was selected on a patient-individual basis before randomisation at Visit 2 by the Investigator, considering comorbidities, concomitant medication, intolerances, previous experiences, and preferences of the patient. During the course of the study, the opioid therapy was gradually optimised to the individual patient needs (dose escalation, opioid rotation, or termination of therapy). This approach allowed to study the benefits of VER-01 compared to a patient-specific optimised opioid therapy taking into account all authorised opioids available on the market. Due to the large number of available opioids, dosage forms, and potencies, blinding was not possible, and an open-label design was chosen.

Actual start date of recruitment	10 March 2023
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 55
Country: Number of subjects enrolled	Spain: 91
Country: Number of subjects enrolled	Czechia: 61
Country: Number of subjects enrolled	Germany: 168
Worldwide total number of subjects	375
EEA total number of subjects	375

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)	284
From 65 to 84 years	90
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall, 508 patients were screened. Out of these, 14 patients were re-screened, resulting in a total of 522 screenings. Of the 508 screened patients, 124 patients were screen failures. The remaining 384 patients were randomised to receive treatment with VER-01 (192 patients) or Opioid (192 patients).

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	VER-01

Arm description:

VER-01 is a herbal medicinal product consisting of the active pharmaceutical ingredient standardised oleoresin of Cannabis sativa L. folium cum flore, tetrahydrocannabinol (THC)-chemotype (cannabis leaves and flowers).

Arm type	Experimental
Investigational medicinal product name	VER-01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Dose: Following patient-individual optimal dose finding in a 3-week Titration Phase, dosing twice per day (morning and evening) with a minimum daily dose of 1 dose unit (2.5 mg THC), a maximum daily dose of 13 dose units (32.5 mg), and a maximum single dose of 8 dose units (20 mg THC); in case of a daily dose of 1 dose unit, intake once daily in the evening.

Mode of administration: Oral administration

Duration of treatment: Approximately 27 weeks: a 3-week Titration Phase and a 24-week Treatment Phase.

Arm title	Opioid
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Arm description:

Opioid therapy was selected by the investigator individually for each patient at Visit 1 prior to randomisation to ensure that the outcome of the randomisation would not influence the opioid selection. The opioid selection was based on the country-specific standard of care and opioids provided for this study by the Sponsor.

Arm type	Active comparator
Investigational medicinal product name	Opioid
Investigational medicinal product code	
Other name	Possible opioids: Tilidine/Naloxone, Tramadol, Fentanyl, Oxycodone, Oxycodone / Naloxone, Hydromorphone, Morphine, Tapentadol, Buprenorphine
Pharmaceutical forms	Prolonged-release tablet, Transdermal patch
Routes of administration	Oral use, Transdermal use

Dosage and administration details:

Dose: Following patient-individual optimal dose finding according to the SmPC of the marketed opioid chosen by the Investigator, daily dosage according to the SmPC of the used opioid therapy.

Mode of administration: The route of administration (oral or transdermal) was chosen by the Investigator at Visit 1.

Duration of treatment: Approximately 27 weeks: a 3-week Titration Phase and a 24-week Treatment Phase.

Number of subjects in period 1	VER-01	Opioid
Started	189	186
Completed	140	126
Not completed	49	60
Consent withdrawn by subject	6	10
Physician decision	2	1
Adverse event, non-fatal	24	26
Other	1	1
Lost to follow-up	1	6
Lack of efficacy	4	8
Protocol deviation	3	-
Withdrawal by subject	8	8

Baseline characteristics

Reporting groups

Reporting group title	VER-01
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Reporting group description:

VER-01 is a herbal medicinal product consisting of the active pharmaceutical ingredient standardised oleoresin of Cannabis sativa L. folium cum flore, tetrahydrocannabinol (THC)-chemotype (cannabis leaves and flowers).

Reporting group title	Opioid
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Reporting group description:

Opioid therapy was selected by the investigator individually for each patient at Visit 1 prior to randomisation to ensure that the outcome of the randomisation would not influence the opioid selection. The opioid selection was based on the country-specific standard of care and opioids provided for this study by the Sponsor.

Reporting group values	VER-01	Opioid	Total
Number of subjects	189	186	375
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	148	136	284
From 65-84 years	41	49	90
85 years and over	0	1	1
Age continuous Units: years			
arithmetic mean	53.9	55.7	
standard deviation	± 13.6	± 12.9	-
Gender categorical Units: Subjects			
Female	118	113	231
Male	71	73	144

End points

End points reporting groups

Reporting group title	VER-01
Reporting group description: VER-01 is a herbal medicinal product consisting of the active pharmaceutical ingredient standardised oleoresin of Cannabis sativa L. folium cum flore, tetrahydrocannabinol (THC)-chemotype (cannabis leaves and flowers).	
Reporting group title	Opioid
Reporting group description: Opioid therapy was selected by the investigator individually for each patient at Visit 1 prior to randomisation to ensure that the outcome of the randomisation would not influence the opioid selection. The opioid selection was based on the country-specific standard of care and opioids provided for this study by the Sponsor.	

Primary: Number of constipation responders - at Visit 9

End point title	Number of constipation responders - at Visit 9
End point description: At Visit 9, a constipation responder is defined as a patient with: a change from baseline (Visit 2) in BFI total score of at least 15 points at Visit 9 and a BFI total score of more than 28.8 at Visit 9.	
End point type	Primary
End point timeframe: At Visit 9	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	148		
Units: n				
number (not applicable)	3	19		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0003 ^[1]
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.5

Notes:

[1] - Primary estimand:

VER-01 vs. opioids: Effect estimate (SE) = -1.38 (0.51), p= 0.007; estimate = 0.25, 95% CI: [0.09; 0.69]

Neuropathic vs. nociceptive: Effect estimate (SE) = -0.60 (0.49), p= 0.214

Primary: Percentage of constipation responders - at Visit 9

End point title	Percentage of constipation responders - at Visit 9 ^[2]
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End point description:

At Visit 9, a constipation responder is defined as a patient with: a change from baseline (Visit 2) in BFI total score of at least 15 points at Visit 9 and a BFI total score of more than 28.8 at Visit 9.

End point type	Primary
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End point timeframe:

At Visit 9

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The statistical analysis specified for the primary endpoint, "Number of constipation responders," also applies to the "Percentage of constipation responders," as the analyses are identical.

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	148		
Units: Percentage of patients				
number (not applicable)	1.9	12.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of 30% / 50% pain responders

End point title	Number of 30% / 50% pain responders
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End point description:

Number of 30% pain responders at Week 27 = Key secondary endpoint

End point type	Secondary
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End point timeframe:

Baseline compared to Week 15 / 27

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[3]	141 ^[4]		
Units: responders				
30% pain responders, Week 15	84	72		
30% pain responders, Week 27	86	71		
50% pain responders, Week 15	59	47		
50% pain responders, Week 27	56	47		

Notes:

[3] - Week 27: 139

[4] - Week 27: 119

Statistical analyses

Statistical analysis title	30% pain responders, Week 15
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.37

Statistical analysis title	30% pain responders, Week 27
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7174 ^[5]
Method	Chi-squared

Notes:

[5] - Common risk difference: Estimate = 0.44, p = 0.430, 95% CI: [-0.07;0.15]

Statistical analysis title	50% pain responders, Week 15
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.61

Statistical analysis title	50% pain responders, Week 27
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.38

Secondary: Percentage of 30% / 50% pain responders

End point title	Percentage of 30% / 50% pain responders
End point description:	
Percentage of 30% pain responders at Week 27 = Key secondary endpoint	
End point type	Secondary
End point timeframe:	
Baseline compared to Week 15 / 27	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[6]	141 ^[7]		
Units: %				
number (not applicable)				
30% pain responders, Week 15	56.4	51.1		
30% pain responders, Week 27	61.9	59.7		
50% pain responders, Week 15	39.6	33.3		
50% pain responders, Week 27	40.3	39.5		

Notes:

[6] - Week 27: 139

[7] - Week 27: 119

Statistical analyses

No statistical analyses for this end point

Secondary: Number of 30% / 50% pain responders - neuropathic pain subgroup

End point title	Number of 30% / 50% pain responders - neuropathic pain subgroup
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End point description:

Number of 30% pain responders from Baseline to Week 27 = Key secondary endpoint

End point type	Secondary
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End point timeframe:

Baseline compared to Week 15 / 27

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46 ^[8]	44 ^[9]		
Units: responders				
30% pain responders, Week 15	26	25		
30% pain responders, Week 27	27	26		
50% pain responders, Week 15	24	18		
50% pain responders, Week 27	20	18		

Notes:

[8] - Week 27: 45

[9] - Week 27: 38

Statistical analyses

Statistical analysis title	30% pain responders, Week 15
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.43

Statistical analysis title	30% pain responders, Week 27
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4263 ^[10]
Method	Chi-squared

Notes:

[10] - Common risk difference: Estimate = 0.01, p = 0.895, 95% CI: [-0.18; 0.21]

Statistical analysis title	50% pain responders, Week 15
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	2

Statistical analysis title	50% pain responders, Week 27
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.5

Secondary: Percentage of 30% / 50% pain responders - neuropathic pain subgroup	
End point title	Percentage of 30% / 50% pain responders - neuropathic pain subgroup
End point description:	
Percentage of 30% pain responders at Week 27 = Key secondary endpoint	
End point type	Secondary
End point timeframe:	
Baseline compared to Week 15 / 27	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46 ^[11]	44 ^[12]		
Units: %				
number (not applicable)				
30% pain responders, Week 15	56.5	56.8		
30% pain responders, Week 27	60.0	68.4		
50% pain responders, Week 15	52.2	40.9		

50% pain responders, Week 27	44.4	47.4		
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Notes:

[11] - Week 27: 45

[12] - Week 27: 38

Statistical analyses

No statistical analyses for this end point

Secondary: Number of 30% / 50% sleep quality responders

End point title	Number of 30% / 50% sleep quality responders
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End point description:

Number of patients with a 30% / 50% improvement of the mean daily low back pain interference with sleep score evaluated on an 11-point NRS;

Number of 30% pain responders at Week 27 = Key secondary endpoint

End point type	Secondary
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End point timeframe:

Baseline compared to Week 15 / 27

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[13]	139 ^[14]		
Units: responders				
30% sleep quality responders, Week 15	100	88		
30% sleep quality responders, Week 27	104	84		
50% sleep quality responders, Week 15	78	59		
50% sleep quality responders, Week 27	67	61		

Notes:

[13] - Week 27: 139

[14] - Week 27: 117

Statistical analyses

Statistical analysis title	30% sleep quality responders, Week 15
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.25

Statistical analysis title	30% sleep quality responders, Week 27
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.21

Statistical analysis title	50% sleep quality responders, Week 15
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.57

Statistical analysis title	50% sleep quality responders, Week 27
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.18

Secondary: Percentage of 30% / 50% sleep quality responders

End point title	Percentage of 30% / 50% sleep quality responders
End point description:	
Number of patients with a 30% / 50% improvement of the mean daily low back pain interference with sleep score evaluated on an 11-point NRS;	
Percentage of 30% pain responders at Week 27 = Key secondary endpoint	
End point type	Secondary
End point timeframe:	
Baseline compared to Week 15 / 27	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[15]	139 ^[16]		
Units: %				
number (not applicable)				
30% sleep quality responders, Week 15	66.7	63.3		
30% sleep quality responders, Week 27	74.8	71.8		
50% sleep quality responders, Week 15	52.0	42.4		
50% sleep quality responders, Week 27	48.2	52.1		

Notes:

[15] - Week 27: 139

[16] - Week 27: 117

Statistical analyses

No statistical analyses for this end point

Secondary: Number of constipation responders - at Visit 6

End point title	Number of constipation responders - at Visit 6
End point description:	
A Visit 6, a constipation responder is defined as a patient with: a change from baseline (Visit 2) in BFI total score of at least 15 points at Visit 6 and a BFI total score of more than 28.8 at Visit 6.	
End point type	Secondary
End point timeframe:	
At Visit 6 after 12 weeks treatment	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	155		
Units: responders	5	18		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid

Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.69

Secondary: Proportion of constipation responders - at Visit 6

End point title	Proportion of constipation responders - at Visit 6
End point description:	A Visit 6, a constipation responder is defined as a patient with: a change from baseline (Visit 2) in BFI total score of at least 15 points at Visit 6 and a BFI total score of more than 28.8 at Visit 6.
End point type	Secondary
End point timeframe:	
At Visit 6 after 12 weeks treatment	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	155		
Units: %				
number (not applicable)	3.0	11.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in BFI subscores - at Visit 6 (Summary of ANCOVA)

End point title	Change from baseline in BFI subscores - at Visit 6 (Summary of ANCOVA)
End point description:	The BFI is an average of three patient-reported scores (each on a 0-100 scale) for the ease of defecation, the feeling of incomplete evacuation, and the personal judgment of constipation.
End point type	Secondary
End point timeframe:	
At Visit 6	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	152		
Units: Points				
least squares mean (standard error)				
Ease of defecation	1.34 (± 1.11)	5.20 (± 1.15)		
Feeling of incomplete bowel evacuation	0.78 (± 0.99)	4.53 (± 1.03)		
Personal judgement of constipation	0.87 (± 1.01)	5.82 (± 1.04)		

Statistical analyses

Statistical analysis title	Ease of defecation
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-3.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.97
upper limit	-0.74
Variability estimate	Standard error of the mean
Dispersion value	1.58

Statistical analysis title	Feeling of incomplete bowel evacuation
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-3.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.52
upper limit	-0.97
Variability estimate	Standard error of the mean
Dispersion value	1.41

Statistical analysis title	Personal judgement of constipation
Comparison groups	VER-01 v Opioid

Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-4.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.77
upper limit	-2.13
Variability estimate	Standard error of the mean
Dispersion value	1.43

Secondary: Change from baseline in BFI subscores - at Visit 9 (Summary of ANCOVA)

End point title	Change from baseline in BFI subscores - at Visit 9 (Summary of ANCOVA)
End point description:	
The BFI is an average of three patient-reported scores (each on a 0-100 scale) for the ease of defecation, the feeling of incomplete evacuation, and the personal judgment of constipation.	
End point type	Secondary
End point timeframe:	
At Visit 9	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	145		
Units: Points				
least squares mean (standard error)				
Ease of defecation	-0.20 (± 1.18)	6.48 (± 1.67)		
Feeling of incomplete bowel evacuation	-0.01 (± 1.14)	6.27 (± 1.18)		
Personal judgement of constipation	0.50 (± 1.23)	7.23 (± 1.27)		

Statistical analyses

Statistical analysis title	Ease of defecation
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-6.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.98
upper limit	-3.39
Variability estimate	Standard error of the mean
Dispersion value	1.67

Statistical analysis title	Feeling of incomplete bowel evacuation
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-6.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.48
upper limit	-3.07
Variability estimate	Standard error of the mean
Dispersion value	1.63

Statistical analysis title	Personal judgement of constipation
Comparison groups	Opioid v VER-01
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-6.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.16
upper limit	-3.3
Variability estimate	Standard error of the mean
Dispersion value	1.74

Secondary: Change from baseline in BFI total score - at Visit 6 (Summary of ANCOVA)

End point title	Change from baseline in BFI total score - at Visit 6 (Summary of ANCOVA)
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End point description:

The BFI is an average of three patient-reported scores (each on a 0-100 scale) for the ease of

defecation, the feeling of incomplete evacuation, and the personal judgment of constipation.

End point type	Secondary
End point timeframe:	
At Visit 6	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	152		
Units: Points				
least squares mean (standard error)	1.13 (\pm 0.95)	5.17 (\pm 0.98)		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-4.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.69
upper limit	-1.38
Variability estimate	Standard error of the mean
Dispersion value	1.35

Secondary: Change from baseline in BFI total score - at Visit 9 (Summary of ANCOVA)

End point title	Change from baseline in BFI total score - at Visit 9 (Summary of ANCOVA)
End point description:	
The BFI is an average of three patient-reported scores (each on a 0-100 scale) for the ease of defecation, the feeling of incomplete evacuation, and the personal judgment of constipation.	
End point type	Secondary
End point timeframe:	
At Visit 9	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	145		
Units: Points				
least squares mean (standard error)	0.27 (\pm 1.09)	6.60 (\pm 1.12)		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-6.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.38
upper limit	-3.3
Variability estimate	Standard error of the mean
Dispersion value	1.54

Secondary: Number of patients with intake of laxatives

End point title	Number of patients with intake of laxatives
End point description:	
End point type	Secondary
End point timeframe:	
From Visit 2 to Visit 9	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	186		
Units: number	11	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with intake of laxatives

End point title	Percentage of patients with intake of laxatives
End point description:	
End point type	Secondary
End point timeframe:	
From Visit 2 to Visit 9	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	186		
Units: %				
number (not applicable)	5.8	17.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with intake of laxatives

End point title	Number of days with intake of laxatives
End point description:	
End point type	Secondary
End point timeframe:	
Between Visit 2 and Visit 9	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	186		
Units: Days				
arithmetic mean (standard deviation)	57.2 (± 84.2)	49.2 (± 63.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean daily low back pain (11-point NRS)

End point title	Change from baseline in mean daily low back pain (11-point NRS)
End point description:	
The numeric rating scale pain intensity ranges from 0 = no pain to 10 = worst pain imaginable.	

End point type	Secondary
End point timeframe:	
Baseline to Week 15 / Week 27	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[17]	141 ^[18]		
Units: Points				
arithmetic mean (standard error)				
Week 15	-2.50 (± 2.00)	-2.26 (± 2.18)		
Week 27	-2.68 (± 1.96)	-2.73 (± 2.12)		

Notes:

[17] - Week 27: 139

[18] - Week 27: 119

Statistical analyses

Statistical analysis title	Week 15
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Week 27
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.54
Variability estimate	Standard error of the mean
Dispersion value	0.25

Secondary: Change from baseline in mean daily low back pain (11-point NRS) - neuropathic pain subgroup

End point title	Change from baseline in mean daily low back pain (11-point NRS) - neuropathic pain subgroup
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End point description:

The numeric rating scale pain intensity ranges from 0 = no pain to 10 = worst pain imaginable.

End point type	Secondary
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End point timeframe:

Baseline to Week 15 / Week 27

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46 ^[19]	44 ^[20]		
Units: Points				
arithmetic mean (standard error)				
Week 15	-2.94 (± 2.08)	-2.36 (± 2.31)		
Week 27	-3.05 (± 1.98)	-2.92 (± 2.22)		

Notes:

[19] - Week 27: 45

[20] - Week 27: 38

Statistical analyses

Statistical analysis title	Week 15
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.51
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.46

Statistical analysis title	Week 27
Comparison groups	Opioid v VER-01

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	0.79
Variability estimate	Standard error of the mean
Dispersion value	0.46

Secondary: Change from baseline pain interference with sleep (11-point NRS)

End point title	Change from baseline pain interference with sleep (11-point NRS)
End point description:	
The numeric rating scale sleep quality ranges from 0 = no interference with sleep to 10 = very strong interference with sleep.	
End point type	Secondary
End point timeframe:	
Baseline to Week 15 / Week 27	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[21]	141 ^[22]		
Units: Points				
arithmetic mean (standard error)				
Week 15	-2.57 (± 2.12)	-2.14 (± 2.14)		
Week 27	-2.72 (± 2.09)	-2.48 (± 2.06)		

Notes:

[21] - Week 27: 139

[22] - Week 27: 119

Statistical analyses

Statistical analysis title	Week 15
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	291
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Week 27
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	291
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.26

Secondary: Change from baseline in EQ-5D-5L - at Visit 6

End point title	Change from baseline in EQ-5D-5L - at Visit 6
End point description:	
EQ-ED-5L = European Quality of Life 5 Dimensions 5 Level	
End point type	Secondary
End point timeframe:	
At Visit 6	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	152		
Units: Points				
arithmetic mean (standard deviation)	0.14 (± 0.17)	0.15 (± 0.23)		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid

Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.02

Secondary: Change from baseline in EQ-5D-5L - at Visit 9

End point title	Change from baseline in EQ-5D-5L - at Visit 9
End point description:	
EQ-ED-5L = European Quality of Life 5 Dimensions 5 Level	
End point type	Secondary
End point timeframe:	
At Visit 9	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	144		
Units: Points				
arithmetic mean (standard error)	0.14 (± 0.19)	0.17 (± 0.22)		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.02

Secondary: Number of patients with a minimal clinically relevant change in the SF-12 subscores - at Visit 6

End point title	Number of patients with a minimal clinically relevant change in the SF-12 subscores - at Visit 6
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End point description:

The SF-12 is a general health questionnaire that consists of 12 questions which investigates the patient's state of health. Minimal clinically relevant change for physical component score = improvement of more than 3.29 points from baseline. Minimal clinically relevant change for mental component score = improvement of more than 3.77 points from baseline

End point type	Secondary
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End point timeframe:

Baseline to Visit 6

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	152		
Units: number of patients				
Physical component summary	117	101		
Mental component summary	51	53		

Statistical analyses

Statistical analysis title	Physical component summary
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.18

Statistical analysis title	Mental component summary
Comparison groups	VER-01 v Opioid

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.24

Secondary: Percentage of patients with a minimal clinically relevant change in the SF-12 subscores - at Visit 6

End point title	Percentage of patients with a minimal clinically relevant change in the SF-12 subscores - at Visit 6
End point description:	The SF-12 is a general health questionnaire that consists of 12 questions which investigates the patient's state of health. Minimal clinically relevant change for physical component score = improvement of more than 3.29 points from baseline. Minimal clinically relevant change for mental component score = improvement of more than 3.77 points from baseline.
End point type	Secondary
End point timeframe:	At Visit 6

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	152		
Units: %				
number (not applicable)				
Physical component summary	72.2	66.4		
Mental component summary	31.5	34.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with a minimal clinically relevant change in the SF-12 subscores - at Visit 9

End point title	Number of patients with a minimal clinically relevant change in the SF-12 subscores - at Visit 9
End point description:	The SF-12 is a general health questionnaire that consists of 12 questions which investigates the patient's state of health. Minimal clinically relevant change for physical component score = improvement of more than 3.29 points from baseline. Minimal clinically relevant change for mental component score = improvement of more than 3.77 points from baseline.
End point type	Secondary

End point timeframe:

At Visit 9

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	144		
Units: number of patients				
Physical component summary	112	105		
Mental component summary	47	52		

Statistical analyses

Statistical analysis title	Physical component summary
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.16

Statistical analysis title	Mental component summary
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.18

Secondary: Percentage of patients with a minimal clinically relevant change in the SF-12 subscores - at Visit 9

End point title	Percentage of patients with a minimal clinically relevant change
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End point description:

The SF-12 is a general health questionnaire that consists of 12 questions which investigates the patient's state of health. Minimal clinically relevant change for physical component score = improvement of more than 3.29 points from baseline. Minimal clinically relevant change for mental component score = improvement of more than 3.77 points from baseline.

End point type	Secondary
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End point timeframe:

At Visit 9

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	144		
Units: %				
number (not applicable)				
Physical component summary	73.7	72.9		
Mental component summary	30.9	36.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Roland Morris Disability Questionnaire - at Visit 6

End point title	Change from baseline in Roland Morris Disability Questionnaire - at Visit 6
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End point description:

The Roland Morris Disability Questionnaire (RMDQ) is a self-administered, validated 24-items questionnaire to assess self-rated physical disability caused by low back pain. Each question marked as "is applicable" is scored with one point. The patient-individual total score is calculated as the sum of the scores and ranges from 0 = "no disability" to 24 = "severe disability".

End point type	Secondary
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End point timeframe:

At Visit 6

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	152		
Units: Points				
arithmetic mean (standard deviation)	-4.5 (\pm 4.6)	-3.7 (\pm 5.1)		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	0.34
Variability estimate	Standard error of the mean
Dispersion value	0.55

Secondary: Change from baseline in Roland Morris Disability Questionnaire - at Visit 9

End point title	Change from baseline in Roland Morris Disability Questionnaire - at Visit 9
End point description: The Roland Morris Disability Questionnaire (RMDQ) is a self-administered, validated 24-items questionnaire to assess self-rated physical disability caused by low back pain. Each question marked as "is applicable" is scored with one point. The patient-individual total score is calculated as the sum of the scores and ranges from 0 = "no disability" to 24 = "severe disability".	
End point type	Secondary
End point timeframe: At Visit 9	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	144		
Units: Points				
arithmetic mean (standard deviation)	-4.6 (± 4.8)	-4.3 (± 5.3)		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid

Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.44
upper limit	0.85
Variability estimate	Standard error of the mean
Dispersion value	0.58

Secondary: Number of patients with a minimal clinically relevant change in the Roland Morris Disability Questionnaire total score - at Visit 6

End point title	Number of patients with a minimal clinically relevant change in the Roland Morris Disability Questionnaire total score - at Visit 6
End point description:	The minimal clinically relevant change is based on the improvement of at least 30% in Roland Morris Disability Questionnaire total score compared to baseline.
End point type	Secondary
End point timeframe:	
Baseline compared to Visit 6	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	150		
Units: number of patients	112	84		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.48

Secondary: Percentage of patients with a minimal clinically relevant change in the Roland Morris Disability Questionnaire total score - at Visit 6

End point title	Percentage of patients with a minimal clinically relevant change in the Roland Morris Disability Questionnaire total score - at Visit 6
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End point description:

The minimal clinically relevant change is based on the improvement of at least 30% in Roland Morris Disability Questionnaire total score compared to baseline.

End point type	Secondary
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End point timeframe:

Baseline compared to Visit 6

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	84		
Units: %				
number (not applicable)	69.6	56.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with a minimal clinically relevant change in the Roland Morris Disability Questionnaire total score - at Visit 9

End point title	Number of patients with a minimal clinically relevant change in the Roland Morris Disability Questionnaire total score - at Visit 9
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End point description:

The minimal clinically relevant change is based on the improvement of at least 30% in Roland Morris Disability Questionnaire total score compared to baseline.

End point type	Secondary
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End point timeframe:

Baseline compared to Visit 9

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	143		
Units: number of patients	100	94		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.18

Secondary: Percentage of patients with a minimal clinically relevant change in the Roland Morris Disability Questionnaire total score - at Visit 9

End point title	Percentage of patients with a minimal clinically relevant change in the Roland Morris Disability Questionnaire total score - at Visit 9
End point description:	The minimal clinically relevant change is based on the improvement of at least 30% in Roland Morris Disability Questionnaire total score compared to baseline.
End point type	Secondary
End point timeframe:	Baseline compared to Visit 9

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	143		
Units: %				
number (not applicable)	65.8	65.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients experiencing meaningful improvement of symptoms (PGIC) - at Visit 6

End point title	Number of patients experiencing meaningful improvement of symptoms (PGIC) - at Visit 6
End point description:	Derived binary scale for clinically relevant improvement of symptoms
End point type	Secondary

End point timeframe:

At Visit 6

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	152		
Units: number of patients	87	74		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	312
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.39

Secondary: Percentage of patients experiencing meaningful improvement of symptoms (PGIC) - at Visit 6

End point title	Percentage of patients experiencing meaningful improvement of symptoms (PGIC) - at Visit 6
End point description:	
Derived binary scale for clinically relevant improvement of symptoms	
End point type	Secondary
End point timeframe:	
At Visit 6	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	152		
Units: %				
number (not applicable)	54.4	48.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients experiencing meaningful improvement of symptoms (PGIC) - at Visit 9

End point title	Number of patients experiencing meaningful improvement of symptoms (PGIC) - at Visit 9
End point description:	
End point type	Secondary
End point timeframe:	
At Visit 9	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	144		
Units: number of patients	82	75		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	Opioid v VER-01
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.28

Secondary: Percentage of patients experiencing meaningful improvement of symptoms (PGIC) - at Visit 9

End point title	Percentage of patients experiencing meaningful improvement of symptoms (PGIC) - at Visit 9
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End point description:

End point type	Secondary
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End point timeframe:

At Visit 9

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	144		
Units: %				
number (not applicable)	53.9	52.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of withdrawal symptoms by Medication Withdrawal Questionnaire (SMWQ) scores - at Visit 10 or Follow-up Visit

End point title	Evaluation of withdrawal symptoms by Medication Withdrawal Questionnaire (SMWQ) scores - at Visit 10 or Follow-up Visit
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End point description:

The SMWQ version 1 consists of 10 items, where each item is scored on a 5-point Likert scale ranging from 0 = "not at all", 1 = "very little", 2 = "a little", 3 = "quite a lot", to 4 = "very much". A total score is calculated as the sum of the 10 items, ranging from 0 to 40. A higher total score means more withdrawal symptoms.

End point type	Secondary
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End point timeframe:

At Visit 10

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	130		
Units: Points				
arithmetic mean (standard deviation)	7.1 (± 6.2)	7.9 (± 6.7)		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
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Comparison groups	VER-01 v Opioid
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Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.78

Secondary: Evaluation of withdrawal symptoms by Medication Withdrawal Questionnaire (SMWQ) scores - at Follow-up Visit

End point title	Evaluation of withdrawal symptoms by Medication Withdrawal Questionnaire (SMWQ) scores - at Follow-up Visit
End point description:	
End point type	Secondary
End point timeframe:	
At Follow-up (end of Wash-out Phase)	

End point values	VER-01	Opioid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	42		
Units: Points				
arithmetic mean (standard deviation)	9.2 (± 6.2)	8.4 (± 4.9)		

Statistical analyses

Statistical analysis title	VER-01 vs Opioid
Comparison groups	VER-01 v Opioid
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	3.8

Variability estimate	Standard error of the mean
Dispersion value	1.5

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-Emergent Adverse Events (TEAEs) 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
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Dictionary version	25.1
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Reporting groups

Reporting group title	VER-01
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Reporting group description: -

Reporting group title	Opioid
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Reporting group description: -

Serious adverse events	VER-01	Opioid	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 189 (4.76%)	8 / 186 (4.30%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Escherichia test positive			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pneumothorax			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			

subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fractured base			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal ischaemia			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal inflammation			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 189 (0.53%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal cyst			

subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 189 (0.00%)	2 / 186 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	VER-01	Opioid	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	138 / 189 (73.02%)	137 / 186 (73.66%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	42 / 189 (22.22%)	21 / 186 (11.29%)	
occurrences (all)	55	25	
Headache			
subjects affected / exposed	22 / 189 (11.64%)	27 / 186 (14.52%)	
occurrences (all)	31	43	
Somnolence			
subjects affected / exposed	12 / 189 (6.35%)	12 / 186 (6.45%)	
occurrences (all)	15	12	
Disturbance in attention			
subjects affected / exposed	12 / 189 (6.35%)	2 / 186 (1.08%)	
occurrences (all)	13	3	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed occurrences (all)	12 / 189 (6.35%) 13	17 / 186 (9.14%) 22	
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	29 / 189 (15.34%) 44	13 / 186 (6.99%) 15	
Gastrointestinal disorders Dry mouth subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	21 / 189 (11.11%) 26 18 / 189 (9.52%) 27 13 / 189 (6.88%) 16 9 / 189 (4.76%) 13 4 / 189 (2.12%) 4	5 / 186 (2.69%) 5 25 / 186 (13.44%) 27 43 / 186 (23.12%) 60 12 / 186 (6.45%) 14 11 / 186 (5.91%) 13	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	10 / 189 (5.29%) 13	11 / 186 (5.91%) 17	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	24 / 189 (12.70%) 31	19 / 186 (10.22%) 23	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2023	Adaptation of layout according to form number CT008-03, Removal of signature for Medical Expert, Adaptation of PI signature page according to form number CT008-03, Clarification of pain group "NO" as "NO/Unclear", Clarification of early study intervention discontinuation in 1.2 Study Scheme, Change of visit window of Visit 1 to 14 (-3) days, Separation of dispensing of opioids and VER-01 as well as of assessment of dosing of concomitant analgetic medication and study intervention in SoA, Clarification that nicotine abuse is not relevant for exclusion criterion 1, Clarification that rescue medication can be taken during Run-in Phase for exclusion criterion 12 and randomisation criterion 6, Exception for patients who discontinue study intervention before Visit 6 regarding valuation of treatment response and eligibility to continue treatment, Clarification of requirements for previous analgesic treatment including clarification of analgesic treatments listed in Table 4, and on prohibited analgesic treatment during the study, Instruction that patients experiencing withdrawal symptoms may receive study intervention outside SoA-specified timepoints, Definition that an AE is any medical event for patients during a clinical study, Correction of spelling mistakes and semantics, capital and lower case, usage of treatment a study intervention

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported