



Clinical trial results:

A Double-blind, Randomized, Placebo-controlled, Parallel-group Trial of the Efficacy and Safety of Nabiximols Oromucosal Spray as Add-on Therapy in Patients With Spasticity Due to Multiple Sclerosis

Summary

EudraCT number	2019-002623-14
Trial protocol	CZ PL GB RO
Global end of trial date	28 February 2023

Results information

Result version number	v1
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	GWSP18023
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04203498
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GW Pharma Ltd
Sponsor organisation address	Sovereign House, Vision Park, Histon, Cambridge, United Kingdom,
Public contact	Director pf Clinical Trial Disclosure & Transparency, GW Pharma Ltd, a Jazz Pharmaceuticals Inc. Company, +1 215-832-3750, ClinicalTrialDisclosure@JazzPharma.com
Scientific contact	Director pf Clinical Trial Disclosure & Transparency, GW Pharma Ltd, a Jazz Pharmaceuticals Inc. Company, +1 215-832-3750, ClinicalTrialDisclosure@JazzPharma.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	28 February 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to establish the efficacy of nabiximols relative to placebo in reducing spasm count as part of the presentation of spasticity when used as adjunctive therapy in patients with MS who have not achieved adequate relief from other antispasticity agents.

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, the ICH Tripartite Guideline for GCP Topic E6(R2), the US Food and Drug Administration regulations relating to GCP and clinical trials, the EU Clinical Trials Directive, the EU GCP Directive, and other applicable laws and regulations.

The protocol, protocol amendments, ICF, investigator brochure, and other relevant documents were submitted to an IRB/IEC by the investigator and reviewed and approved by the IRB/IEC before the study was initiated.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2020
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: 64
Country: Number of subjects enrolled	Czechia: 31
Country: Number of subjects enrolled	Romania: 12
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	139
EEA total number of subjects	107

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)	121
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 139 participants who met all inclusion criteria and no exclusion criteria were randomized to treatment at clinic centers in Czech Republic, Poland, Romania, United Kingdom. and United States; 137 participants received treatment.

Pre-assignment

Screening details:

Participants who provided written informed consent were screened for entry into the trial and a number of assessments/procedures were performed to confirm study eligibility.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Nabiximols

Arm description:

Patients randomized to receive GW-1000-2 (nabiximols) self-administered as an oromucosal spray, in the morning and evening, up to a maximum of 12 sprays per day for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	GW-1000-02
Investigational medicinal product code	
Other name	Nabiximols
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

Self-administered as an oromucosal 1 spray/day (starting dose) and titrated to an optimized dose or to a maximum of 12 sprays/day over the first 14 days of treatment

Arm title	Placebo
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Arm description:

Patients randomized to receive placebo self-administered as an oromucosal spray, in the morning and evening, up to a maximum of 12 sprays per day for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

Self-administered as an oromucosal 1 spray/day (starting dose) and titrated to an optimized dose or to a maximum of 12 sprays/day over the first 14 days of treatment

Number of subjects in period 1	Nabiximols	Placebo
Started	69	70
Completed	55	66
Not completed	14	4
Withdrawal of patient consent	7	2
Adverse event, non-fatal	4	1
Decision by the investigator, GW, or authority	-	1
Drug not dispensed due to endpoint error	1	-
Did not receive IMP	2	-

Baseline characteristics

Reporting groups

Reporting group title	Nabiximols
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Reporting group description:

Patients randomized to receive GW-1000-2 (nabiximols) self-administered as an oromucosal spray, in the morning and evening, up to a maximum of 12 sprays per day for 12 weeks.

Reporting group title	Placebo
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Reporting group description:

Patients randomized to receive placebo self-administered as an oromucosal spray, in the morning and evening, up to a maximum of 12 sprays per day for 12 weeks.

Reporting group values	Nabiximols	Placebo	Total
Number of subjects	69	70	139
Age categorical			
Units: Subjects			
<18 years	0	0	0
≥18 years to <45 years	14	15	29
≥45 years to <65 years	46	46	92
≥65 years	9	9	18
Age continuous			
Units: years			
arithmetic mean	52.1	53.0	-
standard deviation	± 10.4	± 10.2	-
Gender categorical			
Units: Subjects			
Female	44	52	96
Male	25	18	43
Race/Ethnicity, Customized			
Units: Subjects			
White	64	68	132
Black or African American	3	1	4
Asian	0	0	0
American Indian or Alaska Native	0	0	0
Other	2	1	3

End points

End points reporting groups

Reporting group title	Nabiximols
Reporting group description: Patients randomized to receive GW-1000-2 (nabiximols) self-administered as an oromucosal spray, in the morning and evening, up to a maximum of 12 sprays per day for 12 weeks.	
Reporting group title	Placebo
Reporting group description: Patients randomized to receive placebo self-administered as an oromucosal spray, in the morning and evening, up to a maximum of 12 sprays per day for 12 weeks.	

Primary: Change in Average Daily Spasm Count From Baseline to Week 12 By 4-Week Period During the 12-Week Randomized Period

End point title	Change in Average Daily Spasm Count From Baseline to Week 12 By 4-Week Period During the 12-Week Randomized Period
End point description: The change in the average daily spasm count was assessed compared to the baseline period.	
End point type	Primary
End point timeframe: Baseline to Week 12	

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	70		
Units: daily spasm count				
least squares mean (standard error)				
Week 1 to 4	-2.23 (± 0.412)	-1.62 (± 0.394)		
Week 5 to 8	-3.42 (± 0.607)	-2.62 (± 0.583)		
Week 9 to 12	-3.84 (± 0.689)	-3.11 (± 0.659)		

Statistical analyses

Statistical analysis title	Nabiximols (Week 9 to 12) vs Placebo
Statistical analysis description: Week 9 to 12 (primary outcome statistics)	
Comparison groups	Nabiximols v Placebo

Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4263
Method	Linear mixed model repeated measures
Parameter estimate	Difference in least squares means
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.54
upper limit	1.08
Variability estimate	Standard error of the mean
Dispersion value	0.914

Secondary: Change in Multiple Sclerosis Spasticity Scale (MSSS-88) Total Score

End point title	Change in Multiple Sclerosis Spasticity Scale (MSSS-88) Total Score
End point description:	
<p>The MSSS-88 is a self-reported measure of the impact of spasticity (muscle stiffness and spasms) in MS. This 88-item scale captures the patient experience and impact of spasticity, including muscle stiffness, pain and discomfort, muscle spasms, effect on daily activities, ability to walk, body movement, patient feelings, and social functioning. Responses to individual questions can range from "1 - not at all bothered" to "4 - extremely bothered." Scores are summed and higher scores indicate poor clinical outcome. Least square means are being reported.</p>	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	54		
Units: unit on a scale				
least squares mean (standard error)				
Week 8	-21.64 (± 5.775)	-26.11 (± 5.461)		
Week 12	-26.53 (± 5.807)	-23.18 (± 5.426)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Laboratory Test Values

End point title	Change From Baseline in Clinical Laboratory Test Values
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End point description:

End point type Secondary

End point timeframe:

Baseline up to Week 12

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	62		
Units: 10 ⁹ cells/liter				
arithmetic mean (standard deviation)				
Basophils	-0.009 (± 0.030)	0.002 (± 0.037)		
Eosinophils	-0.007 (± 0.110)	0.006 (± 0.086)		
Leukocytes	0.146 (± 1.095)	0.139 (± 1.881)		
Lymphocytes	-0.056 (± 0.368)	0.009 (± 0.315)		
Monocytes	0 (± 0.120)	0.001 (± 0.126)		
Neutrophils	0.217 (± 1.004)	0.083 (± 1.788)		
Platelets	-0.085 (± 42.392)	5.290 (± 49.972)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Reporting Any Treatment-emergent Adverse Events

End point title Number of Patients Reporting Any Treatment-emergent Adverse Events

End point description:

A TEAE is an adverse event that started, or worsened in severity or seriousness, following the first dose of the investigational medicinal product.

End point type Secondary

End point timeframe:

From date of first dose of IMP up to 30 days after last dose, up to approximately 16 weeks

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	70		
Units: patients	47	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Erythrocytes

End point title	Change From Baseline in Erythrocytes
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End point description:

End point type	Secondary
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End point timeframe:

Baseline up to Week 12

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	62		
Units: 10 ¹² cells/liter				
arithmetic mean (standard deviation)	0.010 (± 0.241)	-0.007 (± 0.251)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hemoglobin

End point title	Change From Baseline in Hemoglobin
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End point description:

End point type	Secondary
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End point timeframe:

Baseline up to Week 12

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	62		
Units: g/dL				
arithmetic mean (standard deviation)	-0.025 (\pm 0.735)	-0.021 (\pm 0.726)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Erythrocyte Mean Corpuscular Hemoglobin

End point title	Change From Baseline in Erythrocyte Mean Corpuscular Hemoglobin
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	62		
Units: pg				
arithmetic mean (standard deviation)	-0.156 (\pm 0.608)	-0.005 (\pm 0.881)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematocrit Ratio

End point title	Change From Baseline in Hematocrit Ratio
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	62		
Units: ratio of packed cells to total volume				
arithmetic mean (standard deviation)	-0.002 (\pm 0.025)	-0.002 (\pm 0.027)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Blood Pressure

End point title	Change From Baseline in Blood Pressure
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	67		
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic blood pressure	-1.6 (\pm 10.95)	2.6 (\pm 11.31)		
Diastolic blood pressure	0.3 (\pm 8.20)	2.7 (\pm 13.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Heart Rate

End point title	Change From Baseline in Heart Rate
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	67		
Units: beats/minute				
arithmetic mean (standard deviation)	2.5 (\pm 7.70)	0.4 (\pm 10.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Electrocardiogram Parameters

End point title | Change From Baseline in Electrocardiogram Parameters

End point description:

End point type | Secondary

End point timeframe:

Baseline up to Week 12

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	67		
Units: msec				
arithmetic mean (standard deviation)				
PR interval, aggregate	5.5 (\pm 20.51)	1.3 (\pm 21.05)		
QRS duration	1.9 (\pm 9.89)	-6.5 (\pm 37.08)		
QTcB interval	1.5 (\pm 29.58)	-2.4 (\pm 33.29)		
QTcF interval	2.9 (\pm 26.69)	-3.2 (\pm 32.40)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Weight

End point title | Change from Baseline in Weight

End point description:

End point type | Secondary

End point timeframe:

Baseline up to Week 12

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	67		
Units: kg				
arithmetic mean (standard deviation)	-0.338 (\pm 3.198)	-0.394 (\pm 3.578)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Electrocardiogram Pulse Rate

End point title	Change From Baseline in Electrocardiogram Pulse Rate
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End point description:

End point type	Secondary
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End point timeframe:

Baseline up to Week 12

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	67		
Units: beats/min				
arithmetic mean (standard deviation)	-2.6 (\pm 10.21)	0.5 (\pm 8.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Body Mass Index

End point title	Change in Body Mass Index
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End point description:

End point type	Secondary
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End point timeframe:

Baseline up to Week 12

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	67		
Units: kg/m ²				
arithmetic mean (standard deviation)	-0.086 (± 1.052)	-0.159 (± 1.287)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With Suicidal Ideation or Behavior Based on Columbia-Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Patients With Suicidal Ideation or Behavior Based on Columbia-Suicide Severity Rating Scale (C-SSRS)
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End point description:

The C-SSRS is a short questionnaire that is used to assess suicidal ideation (5 questions) and behavior (5 questions) since last patient visit. The questionnaire is completed by participants answering yes or no to each question.

End point type	Secondary
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End point timeframe:

Screening up to Week 12

End point values	Nabiximols	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	70		
Units: number of patients				
Screening: Ideation, Wish to be dead	1	1		
Screening: Ideation, Non-specific active thoughts	1	1		
Screening: Ideation, Active any method no intent	0	1		
Screening: Ideation, Active intent to act, no plan	0	0		
Screening: Ideation, Active specific plan/intent	0	0		
Screening: Behavior, Preparatory acts or behavior	0	0		
Screening: Behavior, Aborted attempt	0	0		
Screening: Behavior, Interrupted attempt	0	0		
Screening: Behavior, Actual attempt	0	1		
Screening: Behavior, Completed suicide	0	0		
Screening: Suicidal ideation or behavior	1	1		
Screening: Self-injurious behavior	0	0		
Baseline: Ideation, Wish to be dead	0	0		
Baseline: Ideation, Non-specific active thoughts	0	0		
Baseline: Ideation, Active any method no intent	0	0		

Baseline: Ideation, Active intent to act, no plan	0	0		
Baseline: Ideation, Active specific plan/intent	0	0		
Baseline: Behavior, Preparatory acts or behavior	0	0		
Baseline: Behavior, Aborted attempt	0	0		
Baseline: Behavior, Interrupted attempt	0	0		
Baseline: Behavior, Actual attempt	0	0		
Baseline: Behavior, Completed suicide	0	0		
Baseline: Suicidal ideation or behavior	0	0		
Baseline: Self-injurious behavior	0	0		
Week 2: Ideation, Wish to be dead	1	0		
Week 2: Ideation, Non-specific active thoughts	0	0		
Week 2: Ideation, Active any method no intent	0	0		
Week 2: Ideation, Active intent to act, no plan	0	0		
Week 2: Ideation, Active specific plan/intent	0	0		
Week 2: Behavior, Preparatory acts or behavior	0	0		
Week 2: Behavior, Aborted attempt	0	0		
Week 2: Behavior, Interrupted attempt	0	0		
Week 2: Behavior, Actual attempt	0	0		
Week 2: Behavior, Completed suicide	0	0		
Week 2: Suicidal ideation or behavior	1	0		
Week 2: Self-injurious behavior	0	0		
Week 4: Ideation, Wish to be dead	0	0		
Week 4: Ideation, Non-specific active thoughts	0	0		
Week 4: Ideation, Active any method no intent	0	0		
Week 4: Ideation, Active intent to act, no plan	0	0		
Week 4: Ideation, Active specific plan/intent	0	0		
Week 4: Behavior, Preparatory acts or behavior	0	0		
Week 4: Behavior, Aborted attempt	0	0		
Week 4: Behavior, Interrupted attempt	0	0		
Week 4: Behavior, Actual attempt	0	0		
Week 4: Behavior, Completed suicide	0	0		
Week 4: Suicidal ideation or behavior	0	0		
Week 4: Self-injurious behavior	0	0		
Week 8: Ideation, Wish to be dead	0	0		
Week 8: Ideation, Non-specific active thoughts	0	0		
Week 8: Ideation, Active any method no intent	0	0		
Week 8: Ideation, Active intent to act, no plan	0	0		
Week 8: Ideation, Active specific plan/intent	0	0		
Week 8: Behavior, Preparatory acts or behavior	0	0		
Week 8: Behavior, Aborted attempt	0	0		

Week 8: Behavior, Interrupted attempt	0	0		
Week 8: Behavior, Actual attempt	0	0		
Week 8: Behavior, Completed suicide	0	0		
Week 8: Suicidal ideation or behavior	0	0		
Week 8: Self-injurious behavior	0	0		
Week 12: Ideation, Wish to be dead	0	0		
Week 12: Ideation, Non-specific active thoughts	0	0		
Week 12: Ideation, Active any method no intent	0	0		
Week 12: Ideation, Active intent to act, no plan	0	0		
Week 12: Ideation, Active specific plan/intent	0	0		
Week 12: Behavior, Preparatory acts or behavior	0	0		
Week 12: Behavior, Aborted attempt	0	0		
Week 12: Behavior, Interrupted attempt	0	0		
Week 12: Behavior, Actual attempt	0	0		
Week 12: Behavior, Completed suicide	0	0		
Week 12: Suicidal ideation or behavior	0	0		
Week 12: Self-injurious behavior	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from baseline up to end of study, approximately 2 years 5 months.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Patients randomized to receive placebo self-administered as an oromucosal spray in the morning and evening, up to a maximum of 12 sprays per day for 12 weeks.

Reporting group title	Nabiximols
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Reporting group description:

Patients randomized to receive GW-1000-2 (nabiximols) self-administered as an oromucosal spray in the morning and evening, up to a maximum of 12 sprays per day for 12 weeks.

Serious adverse events	Placebo	Nabiximols	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 70 (7.14%)	3 / 67 (4.48%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	2 / 70 (2.86%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 70 (2.86%)	2 / 67 (2.99%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			

subjects affected / exposed	1 / 70 (1.43%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Nabiximols	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 70 (27.14%)	46 / 67 (68.66%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 70 (7.14%)	14 / 67 (20.90%)	
occurrences (all)	8	15	
Somnolence			
subjects affected / exposed	2 / 70 (2.86%)	7 / 67 (10.45%)	
occurrences (all)	2	7	
Taste disorder			
subjects affected / exposed	0 / 70 (0.00%)	4 / 67 (5.97%)	
occurrences (all)	0	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 70 (2.86%)	8 / 67 (11.94%)	
occurrences (all)	3	9	
Asthenia			
subjects affected / exposed	2 / 70 (2.86%)	4 / 67 (5.97%)	
occurrences (all)	2	4	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 70 (0.00%)	6 / 67 (8.96%)	
occurrences (all)	0	8	
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	4 / 70 (5.71%) 5	3 / 67 (4.48%) 3	
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	4 / 70 (5.71%) 5	3 / 67 (4.48%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
28 February 2023	The study was terminated based on a business decision by the Sponsor.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study enrollment did not reach the planned number of participants (N=446). In the current analysis, a total of 139 participants were randomized and 137 received treatment.

Notes: