Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, 2-way Crossover Trial to Evaluate the Effect of Nabiximols Oromucosal Spray on Clinical Measures of Spasticity in Patients with Multiple Sclerosis

Summary

EudraCT number	2020-003271-18
Trial protocol	CZ ES
Global end of trial date	11 November 2022

Results information

Result version number	v1 (current)
This version publication date	25 November 2023
First version publication date	25 November 2023

Trial information

Trial identification

Sponsor protocol code	GWSP20105

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04984278
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 Clinical Trial Disclosure & Transparency, GW Pharma Ltd, a Jazz Pharmaceuticals Inc. Company, 1 215-832-3750, ClinicalTrialDisclosure@JazzPharma.com
Scientific contact	Director 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	11 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of multiple doses of nabiximols compared with placebo on a clinical measure of velocity-dependent muscle tone in the lower limbs (Lower Limb Muscle Tone-6; LLMT-6) in patients with MS

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	16 August 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	Poland: 15
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Czechia: 13
Worldwide total number of subjects	31
EEA total number of subjects	30

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)	28
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 31 participants who met all inclusion criteria and no exclusion criteria were randomized to treatment at 7 clinic centers in Poland, Czech Republic, Spain, and United Kingdom.

Pre-assignment

Screening details:

After signing the ICF, participants with spasticity associated with MS participated in a Screening Period of up to 28 days; changes in the dosing regimen of the participants' current MS antispasticity medications, if any, were not made during this period.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Nabiximols First, Then Placebo

Arm description:

Participants who were randomized to receive GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received matching placebo treatment for 21 days (starting at Day 31; Treatment Period 2).

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 spray for 21 days

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 spray for 21 days

Arm title	Placebo First, Then Nabiximols

Arm description:

Participants who were randomized to receive matching placebo self-administered for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 31; Treatment Period 2).

Arm type	Experimental

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 spray for 21 days

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 spray for 21 days

Number of subjects in period 1	Nabiximols First, Then Placebo	Placebo First, Then Nabiximols
Started	16	15
Completed	15	14
Not completed	1	1
Not specified	-	1
Withdrawal by subject	1	-

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Nabiximols First, Then Placebo

Arm description:

Participants who were randomized to receive GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received matching placebo treatment for 21 days (starting at Day 31; Treatment Period 2).

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 spray for 21 days	
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 spray for 21 days	
Arm title	Placebo First, Then Nabiximols
Arm description: Participants who were randomized to receive matching placebo self-administered for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 31; Treatment Period 2).	
Arm type	Experimental
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 spray for 21 days	
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 spray for 21 days	

Number of subjects in period 2	Nabiximols First, Then Placebo	Placebo First, Then Nabiximols
Started	15	14
Completed	14	13
Not completed	1	1
Adverse event, non-fatal	1	-
Not specified	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Nabiximols First, Then Placebo
Reporting group description:	
Participants who were randomized to receive GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received matching placebo treatment for 21 days (starting at Day 31; Treatment Period 2).	
Reporting group title	Placebo First, Then Nabiximols
Reporting group description:	
Participants who were randomized to receive matching placebo self-administered for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 31; Treatment Period 2).	

Reporting group values	Nabiximols First, Then Placebo	Placebo First, Then Nabiximols	Total
Number of subjects	16	15	31
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)	14	14	28
From 65-84 years	2	1	3
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	53.5	48.8	
standard deviation	± 10.3	± 7.4	-
Gender categorical Units: Subjects			
Female	10	9	19
Male	6	6	12

End points

End points reporting groups

Reporting group title	Nabiximols First, Then Placebo

Reporting group description:

Participants who were randomized to receive GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received matching placebo treatment for 21 days (starting at Day 31; Treatment Period 2).

Reporting group title	Placebo First, Then Nabiximols

Reporting group description:

Participants who were randomized to receive matching placebo self-administered for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 31; Treatment Period 2).

Reporting group title	Nabiximols First, Then Placebo

Reporting group description:

Participants who were randomized to receive GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received matching placebo treatment for 21 days (starting at Day 31; Treatment Period 2).

Reporting group title	Placebo First, Then Nabiximols

Reporting group description:

Participants who were randomized to receive matching placebo self-administered for 21 days (starting on Day 1; Treatment Period 1), followed by at least a 7-day wash out period, and then received GW-1000-02 (nabiximols) self-administered as an oromucosal spray for 21 days (starting on Day 31; Treatment Period 2).

Subject analysis set title	Nabiximols
Subject analysis set type	Full analysis

Subject analysis set description:

A 21-day treatment period with nabiximols self-administered as an oromucosal spray (without regard to treatment period).

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

A 21-day treatment period with placebo self-administered as an oromucosal spray (without regard to treatment period).

Subject analysis set title	Nabiximols
Subject analysis set type	Safety analysis

Subject analysis set description:

A 21-day treatment period with nabiximols self-administered as an oromucosal spray (without regard to treatment period).

Subject analysis set title	Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

A 21-day treatment period with placebo self-administered as an oromucosal spray (without regard to treatment period).

Primary: Change From Baseline in Lower Limb Muscle Tone-6 (LLMT-6)

End point title	Change From Baseline in Lower Limb Muscle Tone-6 (LLMT-6)

End point description:

LLMT-6 is defined as the average of the 6 individual Modified Ashworth Scale (MAS) transformed scores of knee flexors, knee extensors, and plantar flexors on both sides of the body. Transformed MAS ranges from 0 (no increase in muscle tone) to 5 (affected part rigid in flexion or extension). The combined (treatment period 1 and treatment period 2) least square mean change from baseline in LLMT-6 score is being reported. Negative values indicate an improvement in muscle tone.

End point type	Primary

End point timeframe:

Baseline (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	15		
Units: units on a scale				
least squares mean (standard error)				
LLMT-6	-0.32 (± 0.072)	-0.04 (± 0.075)		

Statistical analyses

Statistical analysis title	Change From Baseline in LLMT-6
Comparison groups	Nabiximols v Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0048
Method	Mixed models analysis
Parameter estimate	Combined least mean square difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.092

Secondary: Change From Baseline in Lower Limb Muscle Tone-4 (LLMT-4)

End point title	Change From Baseline in Lower Limb Muscle Tone-4 (LLMT-4)

End point description:

LLMT-4 is defined as the average of the 4 individual MAS transformed scores of knee flexors and knee extensors on both sides of the body. Transformed MAS ranges from 0 (no increase in muscle tone) to 5 (affected part rigid in flexion or extension). The combined (treatment period 1 and treatment period 2) least square mean change from baseline in LLMT-4 score is being reported. Negative values indicate an improvement in muscle tone.

End point type	Secondary

End point timeframe:

Baseline (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	15		
Units: units on a scale				
least squares mean (standard error)				
LLMT-4	-0.34 (± 0.079)	-0.09 (± 0.082)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With Any Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Patients With Any Treatment-emergent Adverse Events (TEAEs)

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:

Baseline (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: patients				
number (not applicable)				
Any TEAE	19	6		

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 (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	27		
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic blood pressure	-2.5 (± 11.27)	-4.4 (± 8.26)		
Diastolic blood pressure	-1.9 (± 7.74)	-2.8 (± 7.66)		

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 (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	27		
Units: beats/minute				
arithmetic mean (standard deviation)				
Heart rate	0.9 (± 8.97)	-0.1 (± 9.13)		

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

End point description:

End point type	Secondary

End point timeframe:

Baseline (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27[1]	25[2]		
Units: 10^9 cells per liter				
arithmetic mean (standard deviation)				
Leukocytes	0 (± 1.68)	-0.07 (± 1.94)		
Neutrophils	0.071 (± 0.94)	-0.399 (± 0.53)		
Basophils	-0.01 (± 0.07)	0 (± 0.07)		
Eosinophils	0.04 (± 0.22)	0.04 (± 0.19)		
Lymphocytes	-0.041 (± 0.48)	0.033 (± 0.48)		
Monocytes	0.01 (± 0.22)	0.03 (± 0.20)		
Platelets	2.4 (± 23.20)	4.6 (± 25.91)		

Notes:

[1] - Except neutrophils, n=15

[2] - Except neutrophils, n=12

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Erythrocytes

End point title	Change From Baseline in Erythrocytes

End point description:

End point type	Secondary

End point timeframe:

Baseline (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	27		
Units: 10^12 cells per liter				
arithmetic mean (standard deviation)				
Erythrocytes	-0.138 (± 0.20)	-0.09 (± 0.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hemoglobin

End point title	Change From Baseline in Hemoglobin

End point description:

End point type	Secondary

End point timeframe:

Baseline (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: g/dL				
arithmetic mean (standard deviation)				
Hemoglobin	-0.34 (± 0.62)	-0.21 (± 0.53)		

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:

Hematocrit was measured in whole blood samples. The ratio of packed cells to total volume was assessed. Normal ratio ranges from 0.350–0.470 female and 0.400–0.540 male (normal ranges per our central lab), 0.37 (or 37%) to 0.52 (or 52%) in adults. Lower hematocrit ratios indicate worse clinical outcome.

End point type	Secondary

End point timeframe:

Baseline (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: ratio of packed cells to total volume				
arithmetic mean (standard deviation)				
Hematocrit ratio	-0.012 (± 0.0191)	-0.009 (± 0.0191)		

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 (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg				
arithmetic mean (standard deviation)				
Erythrocyte mean corpuscular hemoglobin	0.1 (± 0.64)	0.1 (± 0.57)		

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 (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	27		
Units: msec				
arithmetic mean (standard deviation)				
PR duration	-3.1 (± 27.35)	0.5 (± 26.78)		
QRS duration	2.0 (± 6.10)	1.7 (± 5.54)		
QT interval	5.4 (± 15.35)	4.0 (± 17.79)		
QTcB interval	-0.8 (± 16.04)	4.9 (± 15.20)		
QTcF interval	2.5 (± 12.60)	5.2 (± 13.84)		

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

End point description:

End point type	Secondary

End point timeframe:

Baseline (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2)

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	27		
Units: beats/minute				
arithmetic mean (standard deviation)				
Electrocardiogram pulse rate	-2.0 (± 9.42)	-0.1 (± 7.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Suicidal Ideation or Behavior Based on The Columbia Suicide Severity Rating Scale (CSSRS)

End point title	Number of Participants With Suicidal Ideation or Behavior Based on The Columbia Suicide Severity Rating Scale (CSSRS)

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

End point timeframe:

Baseline, Day 15, and Day 21

End point values	Nabiximols	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: participants				
number (not applicable)				
Baseline: Ideation	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	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 (non-fatal)	0	0		
Baseline: Behavior, Completed suicide	0	0		
Baseline: Ideation or Behavior	0	0		
Baseline: Self-injurious behavior without intent	0	0		
Day 15: Ideation	0	1		
Day 15: Ideation, Wish to be dead	0	0		
Day 15: Ideation, Non-specific active thoughts	0	0		
Day 15: Ideation, Active any method no intent	0	1		
Day 15: Ideation, Active intent to act no plan	0	1		
Day 15: Ideation, Active specific plan/intent	0	0		
Day 15: Behavior	0	0		
Day 15: Behavior, Preparatory acts or behavior	0	0		
Day 15: Behavior, Aborted attempt	0	0		
Day 15: Behavior, Interrupted attempt	0	0		
Day 15: Behavior, Actual attempt (non-fatal)	0	0		
Day 15: Behavior, Completed suicide	0	0		
Day 15: Ideation or behavior	0	0		
Day 15: Self-injurious behavior without intent	0	0		
Day 21: Ideation	0	0		
Day 21: Ideation, Wish to be dead	0	0		
Day 21: Ideation, Non-specific active thoughts	0	0		
Day 21: Ideation, Active any method no intent	0	0		
Day 21: Ideation, Active intent to act no plan	0	0		
Day 21: Ideation, Active specific plan/intent	0	0		

Day 21: Behavior	0	0		
Day 21: Behavior, Preparatory acts or behavior	0	0		
Day 21: Behavior, Aborted attempt	0	0		
Day 21: Behavior, Interrupted attempt	0	0		
Day 21: Behavior, Actual attempt (non-fatal)	0	0		
Day 21: Behavior, Completed suicide	0	0		
Day 21: Ideation or behavior	0	0		
Day 21: Self-injurious behavior without intent	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse event (TEAE) data were collected from baseline (predose Day 1 of Treatment Period 1) up to Day 51 (end of treatment of Treatment Period 2).

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Nabiximols

Reporting group description:

A 21-day treatment period with nabiximols self-administered as an oromucosal spray (without regard to treatment period).

Reporting group title	Placebo

Reporting group description:

A 21-day treatment period with placebo self-administered as an oromucosal spray (without regard to treatment period).

Serious adverse events	Nabiximols	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Nabiximols	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 30 (20.00%)	0 / 30 (0.00%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 30 (13.33%)	0 / 30 (0.00%)	
occurrences (all)	4	0	
Ear and labyrinth disorders			

Vertigo subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0	

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
11 November 2022	The study was terminated based on a business decision by the Sponsor.	-

Notes:

Limitations and caveats

None reported