



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 |
|-----------------------|-----------|

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 |
|------------------|---------|

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 |
|-----------------------|------------|

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.

| 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: | |
| 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. | |
| 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: 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 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 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: Change From Baseline in Erythrocytes

| | |
|-----------------|--------------------------------------|
| End point title | Change From Baseline in Erythrocytes |
|-----------------|--------------------------------------|

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 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 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 Hemoglobin

| | |
|------------------------|------------------------------------|
| End point title | Change From Baseline in 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: 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 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 Electrocardiogram Pulse Rate

| | |
|------------------------|--|
| End point title | Change From Baseline in Electrocardiogram Pulse 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 | 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 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 in Body Mass Index

| | |
|------------------------|---------------------------|
| End point title | Change in Body Mass Index |
| 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/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) |
|-----------------|--|

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:

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 |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| 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.

| | |
|-----------------------|------------|
| 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.

| 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: