



Clinical trial results: Efficacy of Cannabidiol in Treatment of Pain due to symptomatic Osteoarthritis of the Knee: A randomized, double-blind, placebo- controlled

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2019-003591-40 |
| Trial protocol | AT |
| Global end of trial date | 29 March 2022 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 23 October 2024 |
| First version publication date | 23 October 2024 |
| Summary attachment (see zip file) | Cannabidiol Osteoarthritis Knee (CBD_KOA.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | 131082019 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04607603 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Medical University of Vienna |
| Sponsor organisation address | Waehringer Guertel 18-20, Vienna, Austria, |
| Public contact | Universitätsklinik für Anästhesie, Medizinische Universität Wien, +43 14040041440, sibylle.pramhas@meduniwien.ac.at |
| Scientific contact | Universitätsklinik für Anästhesie, Medizinische Universität Wien, +43 14040041440, sibylle.pramhas@meduniwien.ac.at |

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 | 01 December 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 March 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 March 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Primary Objective/Hypothesis

To evaluate the efficacy of cannabidiol in reducing pain due to knee osteoarthritis, as compared to placebo.

Efficacy will be evaluated using the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) Pain score.

Protection of trial subjects:

Informed consent of subjects

Following comprehensive instruction regarding the nature, significance, impact and risks of this clinical trial, the patient must give written consent to participation in the study.

During the instruction the trial participants are to be made aware of the fact that they can withdraw their consent – without giving reasons – at any time without their further medical care being influenced in any way.

In addition to the comprehensive instructions given to the trial participants by the Investigator, the trial participants also receive a written patient information sheet in comprehensible language, explaining the nature and purpose of the study and its progress.

The patients must agree to the possibility of study-related data being passed on to relevant authorities.

The patients must be informed in detail of their obligations in relation to the trial participants insurance in order not to jeopardize insurance cover.

Acknowledgement / approval of the study

The Investigator (or a designated CRO) will submit this protocol and any related document provided to the subject (such as subject information used to obtain informed consent) to an Ethics Committee (EC) or Institutional Review Board (IRB). Approval from the committee must be obtained before starting the study.

The clinical trial shall be performed in full compliance with the legal regulations according to the Drug Law (AMG - Arzneimittelgesetz) of the Republic of Austria.

An application must also be submitted to the Austrian Competent Authorities (Bundesamt für Sicherheit im Gesundheitswesen (BASG) represented by the Agency for Health and Food Safety (AGES Medizinmarktaufsicht) and registered to the European Clinical Trial Database (EudraCT) using the required forms. The timelines for (silent) approval set by national law must be followed before starting the study.

Background therapy:

Paracetamol 3g per die

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 | Austria: 86 |
| Worldwide total number of subjects | 86 |
| EEA total number of subjects | 86 |

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) | 56 |
| From 65 to 84 years | 28 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

Recruitment was conducted from October 1, 2020 to December 16, 2021. Patients were recruited at the Outpatient Clinic of the Department of Special Anaesthesia and Pain Therapy at the Medical University of Vienna, by advertisement in news print and via social media platforms.

Pre-assignment

Screening details:

Patients aged over 18–98 years with chronic knee pain were eligible. Patients were required to score ≥ 5 on the pain subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Patients also had to fulfill the ACR clinical criteria for KOA

Period 1

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

Blinding implementation details:

Study medication for the entire study period was uniformly packaged and numbered by Hubertus Pharmacy (Spittal/Drau, Austria) that was not otherwise involved in the study. All study medication was delivered to Outpatient Clinic of the Department of Special Anaesthesia and Pain Therapy at the Medical University of Vienna prior to the initiation of the study in a single batch. Participants were randomized to receive a medication number.

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cannabidiol |

Arm description:

Hemp-derived CBD (purity >99,8%) was extracted by BioSynthesis Pharma Group (BSPG) Ltd., Sandwich, UK, then imported and formulated into capsules by the BSPG subsidiary Trigal Pharma GmbH, Austria. Cap-sules containing CBD (200 mg/capsule).

Patients in CBD arm received 600mg per die (200mg-200mg-200mg)

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | CBD |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

200mg CBD/capsule
600mg per die (1-1-1)

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Ingredients: Fat, Ascorbyl Pamitate (E304), gelatine capsules (gelatine, titandioxide and/or other approved food colouring) Manufacturer: Hubertus Apotheke, Spital/Drau, Austria

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|----------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

3 per die (1-1-1)

| Number of subjects in period 1 | Cannabidiol | Placebo |
|---------------------------------------|-------------|---------|
| Started | 43 | 43 |
| Completed | 27 | 31 |
| Not completed | 16 | 12 |
| Consent withdrawn by subject | 1 | 1 |
| Adverse event, non-fatal | 9 | 5 |
| Lost to follow-up | 2 | 1 |
| Lack of efficacy | 4 | 1 |
| Protocol deviation | - | 4 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Cannabidiol |
|-----------------------|-------------|

Reporting group description:

Hemp-derived CBD (purity >99,8%) was extracted by BioSynthesis Pharma Group (BSPG) Ltd., Sandwich, UK, then imported and formulated into capsules by the BSPG subsidiary Trigal Pharma GmbH, Austria. Cap-sules containing CBD (200 mg/capsule).

Patients in CBD arm received 600mg per die (200mg-200mg-200mg)

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Ingredients: Fat, Ascorbyl Pamitate (E304), gelatine capsules (gelatine, titandioxide and/or other approved food colouring) Manufacturer: Hubertus Apotheke, Spital/Drau, Austria

| Reporting group values | Cannabidiol | Placebo | Total |
|---------------------------------------|--------------|----------|-------|
| Number of subjects | 43 | 43 | 86 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 34 | 23 | 57 |
| From 65-84 years | 8 | 19 | 27 |
| 85 years and over | 1 | 1 | 2 |
| Age continuous Units: years | | | |
| median | 60.0 | 65 | |
| inter-quartile range (Q1-Q3) | 55.0 to 65.0 | 56 to 73 | - |
| Gender categorical Units: Subjects | | | |
| Female | 30 | 30 | 60 |
| Male | 13 | 13 | 26 |

Subject analysis sets

| | |
|----------------------------|-----|
| Subject analysis set title | CBD |
|----------------------------|-----|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

CBD-Treatment

| | |
|----------------------------|---------|
| Subject analysis set title | Placebo |
|----------------------------|---------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Placebo

| Reporting group values | CBD | Placebo | |
|------------------------------------|-----|---------|--|
| Number of subjects | 43 | 43 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 34 | 23 | |
| From 65-84 years | 8 | 19 | |
| 85 years and over | 1 | 1 | |

| | | | |
|------------------------------|--------------|------------|--|
| Age continuous | | | |
| Units: years | | | |
| median | 60.0 | 65.0 | |
| inter-quartile range (Q1-Q3) | 55.0 to 65.0 | 56.0 to 73 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 30 | 30 | |
| Male | 13 | 13 | |

End points

End points reporting groups

| | |
|--|---------------|
| Reporting group title | Cannabidiol |
| Reporting group description: Hemp-derived CBD (purity >99,8%) was extracted by BioSynthesis Pharma Group (BSPG) Ltd., Sandwich, UK, then imported and formulated into capsules by the BSPG subsidiary Trigal Pharma GmbH, Austria. Cap-sules containing CBD (200 mg/capsule). | |
| Patients in CBD arm received 600mg per die (200mg-200mg-200mg) | |
| Reporting group title | Placebo |
| Reporting group description: Ingredients: Fat, Ascorbyl Pamitate (E304), gelatine capsules (gelatine, titandioxide and/or other approved food colouring) Manufacturer: Hubertus Apotheke, Spital/Drau, Austria | |
| Subject analysis set title | CBD |
| Subject analysis set type | Full analysis |
| Subject analysis set description: CBD-Treatment | |
| Subject analysis set title | Placebo |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Placebo | |

Primary: Change in WOMAC pain subscale score from baseline

| | |
|---------------------------------|---|
| End point title | Change in WOMAC pain subscale score from baseline |
| End point description: | |
| End point type | Primary |
| End point timeframe: 8 weeks | |

| End point values | Cannabidiol | Placebo | | |
|---------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Scale 1-10 | | | | |
| median (inter-quartile range (Q1-Q3)) | 2.5 (1.8 to 3.3) | 2.4 (1.7 to 3.2) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | analysis of covariance model |
| Statistical analysis description: The primary endpoint was analyzed using an analysis of covariance model with change from baseline to week 8 as dependent variable and randomization group, baseline score of WOMAC Pain and stratification variables as independent variables; least-squares means from this model and their group differences are reported with 95% confidence intervals (CI). Residual distributions were successfully checked for approximate | |

normal distribution and potentially influential observations.

| | |
|---|-----------------------|
| Comparison groups | Cannabidiol v Placebo |
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | ANCOVA |

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From the start to the end

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The template requires that number of subjects per reporting group that experienced a non-serious adverse events be given. However we reported total frequency of non-serious adverse per reporting group in our study.

CBD: 39 subjects at least one AE; Placebo 36 subjects at least one AE

Frequencies: CBD Placebo

Diarrhea 19 20

Elevation

of ASAT, ALAT,

gamma-GT 15 5

Abdominal pain 14 11

Fatigue 14 1

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? No

Limitations and caveats

None reported