THC&CBD NeuroCart&PainCart study

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21413

Source
NTR

Brief title
CHDR2048

Health condition

Chronic neuropathic pain, nerve pain, neuralgia

Sponsors and support

Primary sponsor: CHDR
Source(s) of monetary or material Support: CHDR

Intervention

Outcome measures

Primary outcome

NeuroCart test battery:
Body sway:
o antero-posterior sway (mm);
• Visual Analog Scales (VAS) according to Bond and Lader to assess:
o mood (mm),
o alertness (mm), and
o calmness (mm).

• Visual Analog Scales (VAS) according to Bowdle to assess:
o Feeling high (mm)
o Internal perception (mm)
o External perception (mm)
• Stroop colour word
o Stroop card 1, 2 and 3
- Time completing cards (sec)
- Number of incorrect answers of cards
o Stroop effect: difference in reaction time between card 3 and 2 (sec)
• Adaptive Tracking
o Average performance (%);
• Simple Reaction Time Task (SRT)
o Reaction time (ms)

Questionnaires:
• State-Trait Anxiety Inventory (STAI)
o State anxiety score

• Brief Symptom Inventory (BSI)
o General somatic symptoms
o Cognitive symptoms
o Interpersonal sensitivity
o Depressed mood
o Anxiety
o Hostility
o Phobic anxiety
o Paranoid thoughts
o Psychoticism
o Global severity index

Neuroendocrine markers:
• Prolactin (µg/L)
• Cortisol (nmol/L)

Physiological markers:
• Heart rate (bpm)

Secondary outcome

PainCart test battery:
• Thermal Pain (capsaicin sensitized skin and untreated control skin):Pain Detection Threshold (PDT), Area Under the Visual
Analogue Scale(VAS) pain Curve (AUC), VAS, Short Form McGill Pain Questionnaire (SFMPQ)
• McGill MPQ-SF
• Pressure Pain: PDT, PTT, AUC, VAS, SF-MPQ
• Cold Pressor: PDT, PTT, AUC, VAS, SF-MPQ
• Electrical Stair: PDT, PTT, AUC, VAS, SF-MPQ

• Pinprick pain assessment: area of secondary mechanical allodynia
following capsaicin application using von Frey hair filaments

PK parameters of THC (and metabolites: 11-OH-THC, THCCOOH), CBD (and metabolites: 6α-OH-CBD, 6β-OH-CBD, 7-OH-CBD,
7-CBD-COOH and 2'-CBD-Glucuronide) by non-compartmental analysis of the plasma concentration-time data:
• AUCinf, AUClast, CL/F, Cmax, t1/2, tlag, tmax, Vz/F
• Dose-normalized PK parameters: AUCinf, AUClast, Cmax
• Treatment-emergent (serious) adverse events ((S)AEs) throughout the study at every study visit
• Concomitant medication throughout the study at every study visit
• Vital signs (Pulse Rate (bpm), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg)) as per assessment schedule
• Clinical laboratory tests (Hematology, blood chemistry,glucose and urinalysis) as per assessment schedule
• ECG parameters (Heart Rate (HR) (bpm), PR, QRS, QT, QTcB, QTcF) as per assessment schedule

Study description

Background summary

THC shows promise as an analgesic compound for some (although not all) patients with chronic neuropathic pain. However, lack of efficacy in broad patient populations and adverse effects limit the therapeutic potential of THC for chronic neuropathic pain. There is an unmet medical need for a way to improve the tolerability of THC by reducing its adverse effects without compromising its analgesic properties.
There is clinical evidence for CBD counteracting negative effects of THC, although this effect has not been found consistently. There is no consensus yet regarding a beneficial ratio of CBD to THC for clinical practice with regards to improved side-effect profiles, or improved overall therapeutic effects.
The goal of this trial is to investigate whether (and at which dose or ratio) CBD has a modulating effect on the psychotropic effects of THC by comparing the effects of THC to the combination of THC with CBD in a range of ratios. Simultaneously, this study will compare the analgesic effects THC with combinations of THC and CBD. We will measure the psychoactive effects of the study treatments with the validated NeuroCart test battery and the analgesic effects using the validated PainCart test battery. This study is funded by the ZonMW “Goed Gebruik Geneesmiddelen” program. The findings from this study may influence the selection of a THC:CBD ratio in a future trial in patients with chronic neuropathic pain.

Study objective

The goal of this trial is to investigate whether (and at which dose or ratio) CBD has a

modulating effect on the psychotropic effects of THC by comparing the effects of THC to the combination of THC with CBD in a range of ratios. Simultaneously, this study will compare the analgesic effects THC with combinations of THC and CBD. We will measure the psychoactive effects of the study treatments with the validated NeuroCart test battery and the analgesic effects using the validated PainCart test battery.The findings from this study may influence the selection of a THC:CBD ratio in a future trial in patients with chronic neuropathic pain.

Study design

Up to -42 days (Screening) till +7-14 days (Follow Up)

Intervention

Δ9-tetrahydrocannabinol (THC) (Namisol®) and Cannabidiol (CBD) (Arvisol®).
Capsaicin 1% (ethanolic solution).
Placebo.

Contacts

Public
Centre for Human Drug Research
G. J. Groeneveld

+31 71 5246 400
Scientific
Centre for Human Drug Research
G. J. Groeneveld

+31 71 5246 400

Eligibility criteria

Inclusion criteria

1. Signed informed consent prior to any study-mandated procedure.
2. Healthy male or female subjects, 18 to 45 years of age, inclusive at screening.
3. Body mass index (BMI) between 18 and 30 kg/m2, inclusive at screening, and with a minimum weight of 50 kg.
4. All women of childbearing potential and all males must practice effective contraception during the study and be willing and able to continue contraception for at least 90 days after their last dose of study treatment.

5. Has the ability to communicate well with the Investigator in the Dutch language and willing to comply with the study restrictions.
6. Subject is familiar with cannabis use for at least one year. In the previous 6 months, cannabis use of no more than once a month on average, and able to refrain from using cannabinoids from at least 3 weeks prior to the first treatment period to the end of the last study day.

Exclusion criteria

1. Evidence of any active or chronic disease or condition that could interfere with, or for which the treatment of might interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic
blood pressure, pulse rate, body temperature) and 12-lead electrocardiogram (ECG)). Minor deviations from the normal range may be accepted, if judged by the Investigator to have no clinical relevance.
2. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects.
3. Positive Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening.
4. Systolic blood pressure (SBP) greater than 140 or less than 90 mm Hg, and diastolic blood pressure (DBP) greater than 90 or less than 50 mm Hg at screening.
5. Abnormal findings in the resting ECG at screening defined as:
a. QTcF> 450 or < 300 msec for men and QTcF> 470 or < 300 msec for women
b. Notable resting bradycardia (HR < 40 bpm) or tachycardia (HR > 100 bpm)
c. Personal or family history of congenital long QT syndrome or sudden death;
d. ECG with QRS and/or T wave judged to be unfavourable for a consistently accurate QT measurement (e.g., neuromuscular artefact that cannot be readily eliminated, arrhythmias, indistinct QRS onset, low amplitude T wave, merged T- and U-waves, prominent U waves);
e. Evidence of atrial fibrillation, atrial flutter, complete branch block, Wolf-Parkinson-White Syndrome, or cardiac pacemaker
6. Use of any medications (prescription or over-the-counter [OTC]), within 7 days of study drug administration, or less than 5 half-lives (whichever is longer). Exceptions will only be made if the rationale is clearly documented by the investigator.
7. Use of any vitamin, mineral, herbal, and dietary supplements within 7 days of study drug administration, or less than 5 half-lives (whichever is longer). Exceptions will only be made if the rationale is clearly documented by the investigator.
8. Participation in an investigational drug or device study (last dosing of previous study was within 90 days prior to first dosing of this study).
9. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 21 units alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent.

10. Positive test for drugs of abuse at screening or pre-dose.
11. Alcohol will not be allowed from at least 24 hours before screening or pre-dose.
12. Smoker of more than 10 cigarettes per day prior to screening or who use tobacco products equivalent to more than 10 cigarettes per day and unable to abstain from smoking whilst in the unit.
13. Is demonstrating excess in caffeine consumption (more than eight cups of coffee or equivalent per day
14. Any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug, or multiple drug allergies (non-active hay fever is acceptable).
15. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening or intention to donate blood or blood products during the study.
16. If a woman, pregnant, or breast-feeding, or planning to become pregnant during the study.
17. Any known factor, condition, or disease that might interfere with treatment compliance, study conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.
18. Any current, clinically significant, known medical condition in particular any existing conditions that would affect sensitivity to cold (such as atherosclerosis, Raynaud's disease, urticaria, hypothyroidism) or pain (disease that causes pain, hypesthesia, hyperalgesia, allodynia, paraesthesia, neuropathy, etc.);
19. Subjects indicating pain tests intolerable at screening or achieving tolerance at >80% of maximum input intensity for any pain test for cold, pressure and electrical tests.
20. Subject indicating intolerable pain after capsaicin administration at screening.
21. History of cannabis-induced psychosis, schizophrenia or other clinically relevant psychiatric disorders, as judged by the investigator.
22. No secondary mechanical allodynia induced in subject (area of secondary mechanical allodynia = 0 mm2) at screening.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	08-08-2021
Enrollment:	30
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
N.A.

Ethics review

Positive opinion
Date: 22-06-2021
Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 50995
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9543
CCMO	NL77327.056.21
OMON	NL-OMON50995

Study results

Summary results
N.A.