Transvamix (10% THC / 5% CBD) to treat chronic pain in Epidermolysis Bullosa: An explorative randomized, placebo-controlled and double-blind intervention crossover study

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Ethical review	Approved WMO
Status	Pending
Health condition type	Skin and subcutaneous tissue disorders congenital
Study type	Interventional

Summary

ID

NL-OMON51174

Source
ToetsingOnline

Brief title
A study on the effect of Transvamix for pain in adults with EB

Condition

- Skin and subcutaneous tissue disorders congenital

Synonym
Butterfly skin disease, fragile skin disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: DEBRA-UK

Intervention

Keyword: cannabinoids, epidermolysis bullosa, pain, symptoms

Outcome measures

Primary outcome

The effect of Transvamix, relative to placebo measured by a reduction in the pain quality item *unpleasantness* (using the SF-MPQ2) by 30% and 50%.

• A reduction of 30% and 50% of mean pain scores (of the pain quality *unpleasantness*) between Transvamix and placebo group.

Will be measured as the difference in mean scores pre- (baseline) and post-intervention (Transvamix and placebo) for each group using the pain quality item *unpleasantness* from the SF-MPQ2, a 22-item numerical rating scale (NRS 0-10) survey on pain qualities.

Secondary outcome

• The difference of mean scores of pain qualities between Transvamix and placebo.

Will be measured as the difference of the mean of all SF-MPQ2 pain quality items (which have received a score >0 on NRS) between Transvamix and Placebo.

• The difference of mean scores of pain intensity between Transvamix and placebo.

Will be measured as daily changes in pain intensity (1-14 days placebo, 1-14 days Transvamix) using the VAS-Pain ([no pain] 0-100 [worst pain imaginable]

unit scale) for pain intensity. The change score (delta) from baseline to Transvamix (day 14) and Placebo (day 14) will be calculated.

• To determine the effect of Transvamix on pain self-efficacy

Will be measured using the PSEQ survey pre-intervention (1x baseline) and during intervention (1x Transvamix, 1x placebo), a 10-item survey on the ability to continue normal life given ongoing pain.

• The difference of mean scores of pruritus intensity between Transvamix and placebo.

Will be measured as daily changes in pruritus intensity (1-14 days placebo, 1-14 days Transvamix) using the VAS-Pruritus ([no pruritus] 0-100 [worst pruritus imaginable] unit scale) for pruritus intensity. The change score (delta) from baseline to Transvamix (day 14) and Placebo (day 14) will be calculated.

• The difference in brain connectivity of the seed regions (anterior cingulate cortex and amygdala) to the brain cortex between Transvamix and placebo.

Will be measured using voxel-based analysis of blood oxygen-level dependent functional magnetic resonance imaging (fMRI-BOLD).

• To determine sub-side effect threshold maintenance dose achieved of Transvamix during titration and the respective interindividual variability (CV%).

Will be measured as the dose administered on day 14 of placebo and Transvamix interventions. CV% is measured as inter-participant variance of dose achieved on day 14 of placebo and Transvamix interventions.

• To inventorize how many and which participant-experienced adverse-events

during titration and maintenance of Transvamix and the patient reported burden

for each adverse event on numeric rating scale (NRS [not burdensome at all]

0-10 [extremely burdensome]).

Study description

Background summary

There is an unmet need for more effective pain alleviation in EB patients. EB patient anecdotes on the use of cannabinoid-based medicines (CBMs) are in line with current science aimed at assessing the effectiveness of CBMs for chronic pain conditions. Until now evidence on the effectiveness of CBMs is moderate and is inconclusive. As the pain quality item *unpleasantness* delineates EB pain, we hypothesize the modulation of affective pain processing in the brain by way of intervention with Transvamix (a CBM comprising THC and CBD) - objectified by functional magnetic resonance imaging (fMRI).

Study objective

The primary objective is to determine the effect of Transvamix on the pain quality item *unpleasantness*, relative to placebo. Secondary objectives include the assessment of general pain qualities, pain self-efficacy, general pain and pruritus intensity, functional brain connectivity, adverse events and sub-side effect threshold maintenance dose achieved during titration.

Study design

The study is a two-arm randomized, double-blind, placebo controlled, crossover intervention study.

Intervention

All participants will receive Transvamix-oil comprising 100mg/mL THC and 50mg/mL CBD, and placebo, to be administered sublingually by a 1mL dosing syringe.

Study burden and risks

Participants are 16 years or older and mentally competent. They will receive the study intervention Transvamix-oil, a compounded medication (magistrale bereiding) readily available on prescription and is currently used by patients

for various medical indications in the Netherlands. Transvamix-oil can produce side effects that can be discomforting, but are mild, well tolerated, and disappear within 4-8 hours after administration upon which the following dose can be reduced to mitigate the recurrence of side-effects. Participants will undergo 3x 30 minute MRI scans. A daily logbook will be completed at home electronically - pertaining to the dose administered, possible side-effects and pain/pruritus scores. All participant reported outcomes are completed electronically at home.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Clinical diagnosis, supplemented by genetic analysis, immunofluorescent diagnostics or electron microscopy of congenital epidermolysis bullosa (EB). Including the EB types recessive dystrophic EB, dominant dystrophic EB, junctional EB and EB simplex.
- At least 16 years of age from the date of onset of participation.
- Can read and write in the Dutch language.
- Mentally competent and legally able to appreciate informed consent.
- Reporting an average pain or pruritus mean score >=4 on NRS (0-10) averaged throughout the previous week at one of the following times of day: morning, afternoon or evening.
- - Negative COVID-19 testing will be required prior to participation.

Exclusion criteria

- Patients enrolled in other clinical trials that do not allow for a deviation in treatment.
- Have experienced myocardial infarction or clinically significant cardiac dysfunction within the last 12 months or have had a cardiac disorder that, in the opinion of the investigator would have put the participant at risk of a clinically significant arrhythmia or myocardial infarction.
- Patients with known psychotic disorder (including the use of antipsychotic medications), or a history of suicidal ideation.
- Female patients of child-bearing potential and male participants whose partner was of child-bearing potential, unless willing to ensure that they or their partner used effective contraception.
- Patients who have had significantly impaired renal or hepatic function in the last 12 months.
- The patient is currently using or has used cannabis or cannabinoid-based medications within 30 days of study entry and was unwilling to abstain for the duration of the study.
- Patients unwilling or unable to refrain from driving road vehicles and/or using potentially dangerous machinery where sufficient concentration is necessary.
- Patients unable to stay within the Netherlands for the duration of the study period.
- History of addiction and/or hospital admission due to addiction to recreational or pharmaceutical drugs.
- Patients with contradictions for MRI determined through the MRI safety form.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	03-05-2021
Enrollment:	16
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Transvamix (THC 100mg/mL, CBD 50mg/mL)
Generic name:	Bedrocan / Bedrolite (THC 10% / CBD 5%)

Ethics review

Approved WMO

Date:	15-07-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-000103-20-NL
CCMO	NL76471.042.21