Clinical trial results:
The effect of medical cannabis on neuropathic pain and spasticity in patients with Multiple Sclerosis and in patients with spinal cord injury. A multicenter national placebo-controlled trial

Summary

EudraCT number	2018-002315-98
Trial protocol	DK
Global end of trial date	01 March 2022

Results information

Result version number	v1 (current)
This version publication date	13 April 2023
First version publication date	13 April 2023

Trial information

Trial identification

Sponsor protocol code	MedicalcannabisMSSCI2018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus Universitetshospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 165, Aarhus N, Denmark, 8220
Public contact	Neurologi, Aarhus Universitetshospital, 45 7845 4222, krissven@rm.dk
Scientific contact	Neurologi, Aarhus Universitetshospital, 45 7845 4222, krissven@rm.dk

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

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of the cannabinoids THC, CBD and a combination of CBD/THC on central neuropathic pain and spasticity in patients with multiple sclerosis and in patients with spinal cord injury

Protection of trial subjects:

The study was conducted according to the Helsinki Declaration Guidelines and approved by the Danish Medicine Agency (2018071161), the Science Ethics Committee (VEK1-10-72-291-18), the Data Protection Agency (via the Central Denmark Region's internal notification 1-16-02-582-18), and it was registered with the EU Clinical Trials Register EudraCT (2018-002315-98). The study was an investigator-initiated trial that followed the Good Clinical Practice (GCP) guidelines and was monitored by GCP units from Aarhus, Odense, and Copenhagen Universities, Denmark

Background therapy:

-

Evidence for comparator:

-

Actual start date of recruitment	15 August 2018
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	Denmark: 134
Worldwide total number of subjects	134
EEA total number of subjects	134

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)	116

From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with Multiple Sclerosis (MS) and Spinal Cord Injury (SCI) were included between February 2019 and December 2021 at 10 MS clinics and 2 SCI clinics in Denmark

Pre-assignment

Screening details:

489 patients were screened for eligibility, 355 (72.6%) did not meet the inclusion/exclusion criteria (n=173, mostly due to ongoing use of cannabinoid/cannabis/CBM/opioids), or declined to participate (n=202, mainly due to the driving ban (n=88). Screening failure in 7 patients),
In total, 134 patients (27.4% of all screened) were randomised

Pre-assignment period milestones

Number of subjects started	134
Number of subjects completed	134

Period 1

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

Blinding implementation details:

Patients were randomized to treatment with either THC, CBD, THC&CBD, or placebo in a 1:1:1:1 ratio. Glostrup Pharmacy performed the computer-generated randomization list. Block randomization (block sizes 10-15) was used at the three largest sites (Aarhus, Viborg, and Copenhagen). The treatment allocation list was revealed on 1 March 2022 (after the last patient's last visit and closure of the database). The AEs were evaluated before treatment allocation was revealed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

capsules of hard gelatin, white size 1 with hard fat and no active components
Produced at Glostrup Pharmacy , Denmark

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

The maximum daily dose was nine capsules.The daily dose was titrated for three weeks using a standard escalation schedule. If patients experienced an effect at a lower dose or AEs when escalating, individual lower doses were accepted (min. one capsule/day).

Arm title	delta-9-THC

Arm description:

Capsules of hard gelatin (white size 1) with Dronabinol (natural THC) 2.5 mg
Produced at Glostrup Pharmacy , Denmark

Arm type	Experimental

Investigational medicinal product name	Dronabinol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

The maximum daily dose was nine capsules (divided into three daily doses, THC max dose=22.5 mg) The daily dose was titrated for three weeks using a standard escalation schedule. If patients experienced an effect at a lower dose or AEs when escalating, individual lower doses were accepted

Arm title	Cannabidiol (CBD)

Arm description:

Capsules of hard gelatin, white size 1 with Cannabidiol (synthetic CBD) 5 mg
Produced at Glostrup Pharmacy , Denmark

Arm type	Experimental
Investigational medicinal product name	Cannabidiol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

The maximum daily dose was nine capsules (divided into three daily doses, CBD max dose=45 mg). The daily dose was titrated for three weeks using a standard escalation schedule. If patients experienced an effect at a lower dose or AEs when escalating, individual lower doses were accepted (min. one capsule/day).

Arm title	THC/CBD

Arm description:

Capsules of hard gelatin, white size 1 with Dronabinol (natural THC) 2.5 mg AND Cannabidiol (synthetic CBD) 5 mg
Produced at Glostrup Pharmacy Denmark

Arm type	Experimental
Investigational medicinal product name	Dronabinol AND Cannabidiol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

The maximum daily dose was nine capsules (divided into three daily doses, THC max dose=22.5 mg, CBD max dose=45 mg). The daily dose was titrated for three weeks using a standard escalation schedule. If patients experienced an effect at a lower dose or AEs when escalating, individual lower doses were accepted (min. one capsule/day).

Number of subjects in period 1	Placebo	delta-9-THC	Cannabidiol (CBD)
Started	40	32	31
Completed	37	25	30
Not completed	3	7	1
wish to withdraw from treatment	1	-	-
Physician decision	-	-	1
Adverse event, non-fatal	1	5	-
Lack of efficacy	1	1	-

Protocol deviation	-	1	-

Number of subjects in period 1	THC/CBD
Started	31
Completed	26
Not completed	5
wish to withdraw from treatment	-
Physician decision	-
Adverse event, non-fatal	3
Lack of efficacy	-
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
capsules of hard gelatin, white size 1 with hard fat and no active components Produced at Glostrup Pharmacy , Denmark	
Reporting group title	delta-9-THC
Reporting group description:	
Capsules of hard gelatin (white size 1) with Dronabinol (natural THC) 2.5 mg Produced at Glostrup Pharmacy , Denmark	
Reporting group title	Cannabidiol (CBD)
Reporting group description:	
Capsules of hard gelatin, white size 1 with Cannabidiol (synthetic CBD) 5 mg Produced at Glostrup Pharmacy , Denmark	
Reporting group title	THC/CBD
Reporting group description:	
Capsules of hard gelatin, white size 1 with Dronabinol (natural THC) 2.5 mg AND Cannabidiol (synthetic CBD) 5 mg Produced at Glostrup Pharmacy Denmark	

Reporting group values	Placebo	delta-9-THC	Cannabidiol (CBD)
Number of subjects	40	32	31
Age categorical Units: Subjects			
Age continuous Units: years			
geometric mean	52.2	54.1	53
standard deviation	± 10.4	± 10.4	± 9.8
Gender categorical Units: Subjects			
Female	28	21	22
Male	12	11	9
Patient group Units: Subjects			
MS	34	29	26
SCI	6	3	5

Reporting group values	THC/CBD	Total	
Number of subjects	31	134	
Age categorical Units: Subjects			
Age continuous Units: years			
geometric mean	51.1		
standard deviation	± 12.7	-	

Gender categorical Units: Subjects			
Female	28	99	
Male	3	35	
Patient group Units: Subjects			
MS	30	119	
SCI	1	15	

Subject analysis sets	
Subject analysis set title	placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised to placebo	
Subject analysis set title	THC
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised to THC	
Subject analysis set title	CBD
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised to CBD	
Subject analysis set title	THC/CBD
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised to THC/CBD	

Reporting group values	placebo	THC	CBD
Number of subjects	40	32	31
Age categorical Units: Subjects			
Age continuous Units: years			
geometric mean	52.2	54.1	53.0
standard deviation	± 10.4	± 10.4	± 9.8
Gender categorical Units: Subjects			
Female	28	21	22
Male	12	11	9
Patient group Units: Subjects			
MS	34	29	26
SCI	6	3	5

Reporting group values	THC/CBD		
Number of subjects	31		
Age categorical Units: Subjects			

Age continuous Units: years			
geometric mean	51.1		
standard deviation	± 12.7		
Gender categorical Units: Subjects			
Female	28		
Male	3		
Patient group Units: Subjects			
MS	30		
SCI	1		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
capsules of hard gelatin, white size 1 with hard fat and no active components Produced at Glostrup Pharmacy , Denmark	
Reporting group title	delta-9-THC
Reporting group description:	
Capsules of hard gelatin (white size 1) with Dronabinol (natural THC) 2.5 mg Produced at Glostrup Pharmacy , Denmark	
Reporting group title	Cannabidiol (CBD)
Reporting group description:	
Capsules of hard gelatin, white size 1 with Cannabidiol (synthetic CBD) 5 mg Produced at Glostrup Pharmacy , Denmark	
Reporting group title	THC/CBD
Reporting group description:	
Capsules of hard gelatin, white size 1 with Dronabinol (natural THC) 2.5 mg AND Cannabidiol (synthetic CBD) 5 mg Produced at Glostrup Pharmacy Denmark	
Subject analysis set title	placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised to placebo	
Subject analysis set title	THC
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised to THC	
Subject analysis set title	CBD
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised to CBD	
Subject analysis set title	THC/CBD
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised to THC/CBD	

Primary: NRS pain

End point title	NRS pain
End point description:	
Difference in mean pain intensity from baseline Intention to treat: At least one dose of study medication	
End point type	Primary
End point timeframe:	
6 weeks of treatment	

End point values	Placebo	delta-9-THC	Cannabidiol (CBD)	THC/CBD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	24	27	28
Units: 0-10				
geometric mean (standard deviation)	-1.8 (± 1.8)	-1.4 (± 2)	-1.4 (± 1.6)	-1.6 (± 1.8)

Statistical analyses

Statistical analysis title	ANOVA

Statistical analysis description:

Comparison of mean difference in NRS-pain between treatment arms.

Comparison groups	Placebo v delta-9-THC v Cannabidiol (CBD) v THC/CBD
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.74
Method	ANOVA

Notes:

[1] - ANOVA one-way

Primary: NRS spasticity

End point title	NRS spasticity

End point description:

Difference in mean spasticity intensity from baseline

Intention to treat: At least one dose of study medication

End point type	Primary

End point timeframe:

6 weeks

End point values	Placebo	delta-9-THC	Cannabidiol (CBD)	THC/CBD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	25	26	20
Units: 0-10				
geometric mean (standard deviation)	-1.7 (± 2.3)	-1.5 (± 2.0)	-1.3 (± 1.9)	-1.6 (± 2.4)

Statistical analyses

Statistical analysis title	ANOVA

Statistical analysis description:

Comparison of mean difference NRS.spasticity between treatment arms

Comparison groups	Placebo v delta-9-THC v Cannabidiol (CBD) v THC/CBD

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.89
Method	ANOVA

Notes:

[2] - ANOVA one-way

Adverse events

Adverse events information

Timeframe for reporting adverse events:

11 weeks (treatment and follow-up)

Adverse event reporting additional description:

All AEs (weekly in e-diary and at visits/phone consultation) were collected. All AE questionnaires were evaluated by the sponsor site and allocated to "previous reported and unrelated", "unrelated", "possible or certainly related", and "cannot be assessed". An AE was included in the inventory if it was rated "possible" or "certainly related".

Assessment type	Systematic

Dictionary used

Dictionary name	none
Dictionary version	0

Reporting groups

Reporting group title	delta-9-THC
Reporting group description: -	
Reporting group title	Cannabidiol
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	THC/CBD

Reporting group description: -

Serious adverse events	delta-9-THC	Cannabidiol	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 32 (12.50%)	1 / 31 (3.23%)	2 / 40 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 32 (6.25%)	0 / 31 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Gallstone	Additional description: gallstone attack in a patient with known gallstone and history of gallstone attacks		
subjects affected / exposed	0 / 32 (0.00%)	1 / 31 (3.23%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			

subjects affected / exposed	0 / 32 (0.00%)	0 / 31 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 31 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 31 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever	Additional description: unspecific		
subjects affected / exposed	1 / 32 (3.13%)	0 / 31 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	THC/CBD		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Gallstone	Additional description: gallstone attack in a patient with known gallstone and history of gallstone attacks		
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Decubitus ulcer			

subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fever	Additional description: unspecific		
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	delta-9-THC	Cannabidiol	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 32 (78.13%)	19 / 31 (61.29%)	25 / 40 (62.50%)
Investigations			
others			
subjects affected / exposed	7 / 32 (21.88%)	3 / 31 (9.68%)	3 / 40 (7.50%)
occurrences (all)	7	3	3
Cardiac disorders			
Palpitations			
subjects affected / exposed	6 / 32 (18.75%)	2 / 31 (6.45%)	0 / 40 (0.00%)
occurrences (all)	6	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 32 (46.88%)	10 / 31 (32.26%)	13 / 40 (32.50%)
occurrences (all)	15	10	13
Dizziness			

subjects affected / exposed	19 / 32 (59.38%)	5 / 31 (16.13%)	12 / 40 (30.00%)
occurrences (all)	19	5	12
Tiredness/sleepiness			
subjects affected / exposed	17 / 32 (53.13%)	14 / 31 (45.16%)	14 / 40 (35.00%)
occurrences (all)	17	14	14
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	6 / 32 (18.75%)	4 / 31 (12.90%)	4 / 40 (10.00%)
occurrences (all)	6	4	4
Eye disorders			
Visual disturbances			
subjects affected / exposed	5 / 32 (15.63%)	2 / 31 (6.45%)	3 / 40 (7.50%)
occurrences (all)	5	2	3
Gastrointestinal disorders			
mouth dryness			
subjects affected / exposed	17 / 32 (53.13%)	9 / 31 (29.03%)	11 / 40 (27.50%)
occurrences (all)	17	9	11
Stomach ache			
subjects affected / exposed	8 / 32 (25.00%)	6 / 31 (19.35%)	3 / 40 (7.50%)
occurrences (all)	8	6	3
Nausea			
subjects affected / exposed	6 / 32 (18.75%)	5 / 31 (16.13%)	4 / 40 (10.00%)
occurrences (all)	6	5	4
Diarrhoea			
subjects affected / exposed	3 / 32 (9.38%)	0 / 31 (0.00%)	2 / 40 (5.00%)
occurrences (all)	3	0	2
Skin and subcutaneous tissue disorders			
Flushing			
subjects affected / exposed	6 / 32 (18.75%)	1 / 31 (3.23%)	3 / 40 (7.50%)
occurrences (all)	6	1	3
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	2 / 32 (6.25%)	4 / 31 (12.90%)	4 / 40 (10.00%)
occurrences (all)	2	4	4
Nightmare			
subjects affected / exposed	1 / 32 (3.13%)	0 / 31 (0.00%)	1 / 40 (2.50%)
occurrences (all)	1	0	1

Euphoric mood			
subjects affected / exposed	5 / 32 (15.63%)	1 / 31 (3.23%)	1 / 40 (2.50%)
occurrences (all)	5	1	1
Anxiety			
subjects affected / exposed	3 / 32 (9.38%)	2 / 31 (6.45%)	1 / 40 (2.50%)
occurrences (all)	3	2	1
Nervousness			
subjects affected / exposed	2 / 32 (6.25%)	3 / 31 (9.68%)	3 / 40 (7.50%)
occurrences (all)	2	3	3
Hallucination			
subjects affected / exposed	3 / 32 (9.38%)	3 / 31 (9.68%)	1 / 40 (2.50%)
occurrences (all)	3	3	1
Musculoskeletal and connective tissue disorders			
Muscle pain			
subjects affected / exposed	6 / 32 (18.75%)	4 / 31 (12.90%)	10 / 40 (25.00%)
occurrences (all)	6	4	10

Non-serious adverse events	THC/CBD		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 31 (90.32%)		
Investigations			
others			
subjects affected / exposed	14 / 31 (45.16%)		
occurrences (all)	14		
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 31 (41.94%)		
occurrences (all)	13		
Dizziness			
subjects affected / exposed	18 / 31 (58.06%)		
occurrences (all)	18		
Tiredness/sleepiness			

subjects affected / exposed occurrences (all)	17 / 31 (54.84%) 17		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	 4 / 31 (12.90%) 4		
Eye disorders Visual disturbances subjects affected / exposed occurrences (all)	 3 / 31 (9.68%) 3		
Gastrointestinal disorders mouth dryness subjects affected / exposed occurrences (all) Stomach ache subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 21 / 31 (67.74%) 21 6 / 31 (19.35%) 6 11 / 31 (35.48%) 11 7 / 31 (22.58%) 7		
Skin and subcutaneous tissue disorders Flushing subjects affected / exposed occurrences (all)	 2 / 31 (6.45%) 2		
Psychiatric disorders Depressed mood subjects affected / exposed occurrences (all) Nightmare subjects affected / exposed occurrences (all) Euphoric mood subjects affected / exposed occurrences (all)	 2 / 31 (6.45%) 2 2 / 31 (6.45%) 2 4 / 31 (12.90%) 4		

Anxiety subjects affected / exposed occurrences (all) Nervousness subjects affected / exposed occurrences (all) Hallucination subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3 5 / 31 (16.13%) 5 0 / 31 (0.00%) 0		
Musculoskeletal and connective tissue disorders Muscle pain subjects affected / exposed occurrences (all)	6 / 31 (19.35%) 6		

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
18 November 2019	due to additional documentation (GMP)from the laboratory that controlled the study medicine (please note that the documentation was not related to the study medicine)	26 February 2020
11 March 2020	COVID-19 lockdown	28 April 2020

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

we did not reach the planned number of patients, due to the interruptions and the reluctance of patients to participate due to the driving ban during the study, ongoing use of opioids or cannabis/CBM, and other reasons.

Notes: