Clinical trial results:
CANGLIA: Endocannabinoid control of microglia activation as a new therapeutic target in the treatment of schizophrenia

Summary

EudraCT number	2016-003529-41
Trial protocol	NL
Global end of trial date	31 January 2020

Results information

Result version number	v1 (current)
This version publication date	03 December 2021
First version publication date	03 December 2021

Trial information

Trial identification

Sponsor protocol code	ABR58805

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02932605
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center Utrecht
Sponsor organisation address	Heidelberglaan 100, Utrecht, Netherlands, 3584CX
Public contact	Department of Psychiatry, University Medical Center Utrecht, 0031 887556369, m.bossong@umcutrecht.nl
Scientific contact	Department of Psychiatry, University Medical Center Utrecht, 0031 887556369, m.bossong@umcutrecht.nl

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	03 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2020
Global end of trial reached?	Yes
Global end of trial date	31 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare brain function and metabolism as measured with Magnetic Resonance Imaging (MRI) between recent-onset patients with a psychotic disorder who are randomised to CBD and those randomised to placebo.

Protection of trial subjects:

Potential participants were extensively screened before enrolment, including blood and urine tests examining haematology, chemistry, drug use and pregnancy. For blood sampling and MRI standard procedures were followed, which were performed by appropriately trained staff to minimise risks. During study days, participants could have a break whenever needed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 November 2017
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	Netherlands: 32
Worldwide total number of subjects	32
EEA total number of subjects	32

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)	2
Adults (18-64 years)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited in the Netherlands, between August 2018 and December 2019.

Pre-assignment

Screening details:

In total, 48 recent-onset patients with a psychotic disorder (within five years after diagnosis) signed informed consent and were included in the study. 32 of them were deemed eligible to participate, and were randomised to either placebo or CBD treatment. Potential participants were screened for in- and exclusion criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cannabidiol

Arm description: -

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:

study medication was given as three 200 mg capsules taken once daily.

Arm title	Placebo

Arm description: -

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:

Study medication was given as three capsules taken once daily.

Number of subjects in period 1	Cannabidiol	Placebo
Started	16	16
Completed	16	16

Period 2	
Period 2 title	Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Cannabidiol

Arm description: -

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:

study medication was given as three 200 mg capsules taken once daily.

Arm title	Placebo

Arm description: -

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:

Study medication was given as three capsules taken once daily.

Number of subjects in period 2[1]	Cannabidiol	Placebo
Started	16	15
Completed	16	15

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One patient (in the placebo group) withdrew consent during treatment, i.e. in between baseline and follow-up.

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	32	32	
Age categorical			
Patients were between 16 and 39 years old			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	2	2	
Adults (18-64 years)	30	30	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
geometric mean	26		
standard deviation	± 6	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	22	22	

End points

End points reporting groups	
Reporting group title	Cannabidiol
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Cannabidiol
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Prefrontal metabolite concentrations	
End point title	Prefrontal metabolite concentrations
End point description:	
Prefrontal metabolites measured include GABA,Glx (combined measure of glutamine and glutamate), gluthation	
End point type	Primary
End point timeframe:	
Prefrontal metabolite concentrations were measured at baseline and at follow-up	

End point values	Cannabidiol	Placebo	Cannabidiol	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	14	16	14
Units: arbitrary units				
arithmetic mean (standard deviation)				
GABA	1.09 (± 0.11)	1.12 (± 0.1)	1.14 (± 0.16)	1.17 (± 0.14)
Glx	3.47 (± 0.34)	3.39 (± 0.3)	3.56 (± 0.31)	3.56 (± 0.32)
Glutathion	0.94 (± 0.11)	0.93 (± 0.1)	0.92 (± 0.15)	0.87 (± 0.13)

Statistical analyses

Statistical analysis title	ANOVA
Comparison groups	Placebo v Cannabidiol v Cannabidiol v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From randomisation to either treatment arm until the end of the study	
Assessment type	Systematic
Dictionary used	
Dictionary name	no dictionary used
Dictionary version	x
Reporting groups	
Reporting group title	Cannabidiol
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Cannabidiol	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cannabidiol	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	12 / 16 (75.00%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	7 / 16 (43.75%)	6 / 16 (37.50%)	
occurrences (all)	7	6	
General disorders and administration site conditions			
Injury			
subjects affected / exposed	4 / 16 (25.00%)	0 / 16 (0.00%)	
occurrences (all)	4	0	
Infection or disease			
subjects affected / exposed	4 / 16 (25.00%)	2 / 16 (12.50%)	
occurrences (all)	4	2	

MRI incidental finding			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 16 (50.00%)	1 / 16 (6.25%)	
occurrences (all)	8	1	
Abdominal pain			
subjects affected / exposed	4 / 16 (25.00%)	1 / 16 (6.25%)	
occurrences (all)	4	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 16 (12.50%)	
occurrences (all)	1	2	
Emotional disorder			
subjects affected / exposed	2 / 16 (12.50%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Psychotic symptoms			
subjects affected / exposed	1 / 16 (6.25%)	2 / 16 (12.50%)	
occurrences (all)	1	2	

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

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

Please note that this is all preliminary data and that data analyis is ongoing.

Notes: