Clinical trial results:
Cannabidiol as an add-on therapy in treatment-refractory psychotic disorders

Summary

EudraCT number	2013-000240-26
Trial protocol	GB
Global end of trial date	07 August 2015

Results information

Result version number	v1 (current)
This version publication date	30 September 2018
First version publication date	30 September 2018
Summary attachment (see zip file)	FINAL STUDY REPORT (CBD_ADD_IN_FinalReport_Signed.pdf)

Trial information

Trial identification

Sponsor protocol code	CBD_ADD_IN

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Paul Morrison, King's College London, 44 02078480057, paul.morrison@kcl.ac.uk
Scientific contact	Paul Morrison, King's College London, 44 02078480057, paul.morrison@kcl.ac.uk
Sponsor organisation name	South London & Maudsley NHS Foundation Trust
Sponsor organisation address	Bethlem Royal Hospital, Monks Orchard Road, Beckenham, United Kingdom, BR3 3BX
Public contact	Paul Morrison, South London & Maudsley NHS Foundation Trust, 44 02078480057, paul.morrison@kcl.ac.uk
Scientific contact	Paul Morrison, South London & Maudsley NHS Foundation Trust, 44 02078480057, paul.morrison@kcl.ac.uk

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	07 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 July 2015
Global end of trial reached?	Yes
Global end of trial date	07 August 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine whether the addition of the molecule Cannabidiol (CBD) leads to improvement in the severity of core psychotic symptom, in patients experiencing their first psychotic episode who have failed to recover despite treatment with at least one standard anti-psychotic drug.

Protection of trial subjects:

Subjects would continue to be seen by Community Mental Health team.

Background therapy:

Participants will already be prescribed an oral antipsychotic medication (a dopamine-based pharmaceutical) at the time of entry into the study. In the majority of cases, this will be a 2nd generation drug (e.g. amisulpride, risperidone, olanzapine, quetiapine) in line with treatment guidelines in schizophrenia and local prescribing practice.
CBD will be added to the existing dopamine-based treatment regime

Evidence for comparator:

Not applicable

Actual start date of recruitment	25 September 2014
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	United Kingdom: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants recruited from the South London & Maudsley NHS Foundation Trust in the UK between July 2014 and August 2015.

Pre-assignment

Screening details:

Screening visit to include Psychopathology assessments, metabolic assessments, MRI imaging, vital signs including body weight and urine drug screen.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Full study

Arm description:

An open-label, exploratory therapeutic trial of the molecule Cannabidiol in treatment refractory 1st episode psychosis (n=20), focusing on core psychological and metabolic outcomes. Cannabidiol will be added to an existing treatment regime (based on dopamine receptor antagonists) for 6-weeks duration. Clinical data will be collected over the duration of the trial, at 0, 2, 4 and 6 week time points.

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

Dosage and administration details:

Flexible titrated oral dosing as 100mg capsules x n/day (where n =1-8), Range: 200-800mg/day total, in 1-2 divided doses.
Initial starting dose = 4 capsules/day.
Flexible Dosing: If participants experience the 400mg/d dose as being too sedating, the dose will be reduced to 200mg/d. Blood pressure will be monitored before and after the first dosing of the IMP. If after two weeks, the participant tolerates the 400mg/d dose, the dose will be increased to 600mg/d. If after a further two weeks, the participant tolerates the 600mg/d dose, the dose will be increased to 800mg/d.

Number of subjects in period 1	Full study
Started	5
Completed	3
Not completed	2
Physician decision	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	5	5	
Age categorical 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)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Adults Aged 18-60 years	5	5	
Gender categorical Units: Subjects			
Female	0	0	
Male	5	5	

End points

End points reporting groups

Reporting group title	Full study

Reporting group description:

An open-label, exploratory therapeutic trial of the molecule Cannabidiol in treatment refractory 1st episode psychosis (n=20), focusing on core psychological and metabolic outcomes. Cannabidiol will be added to an existing treatment regime (based on dopamine receptor antagonists) for 6-weeks duration. Clinical data will be collected over the duration of the trial, at 0, 2, 4 and 6 week time points.

Primary: Primary Endpoint

End point title	Primary Endpoint[1]

End point description:

Scores on core psychotic symptoms and functioning, as measured by the following scales:
- The Positive & Negative Syndrome Scale, PANSS22 (videotaped interview).
- The Global Assessment of Functioning Scale, GAF
- The Community Assessment of Psychotic Experiences, CAPE-4222
- The Montgomery-Asberg Depression Rating Scale, MAD RS
- The Clinical Global Impression scale, CGI.

End point type	Primary

End point timeframe:

Until end of trial participation for each participant

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Insufficient data for analysis

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Interviews and questionaires				
number (not applicable)				

Notes:

[2] - Insufficient data was obtained for analysis & trial prematurely terminated. PK sampling not done

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Continuous	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	Whole Trial

Reporting group description: -

Serious adverse events	Whole Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Whole Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)		
Gastrointestinal disorders			
Flatulence			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
stomach cramps			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Psychiatric disorders			
Intoxication	Additional description: Dropped out following the 1st study visit due to concerns of intoxicating effects of IMP one day into the trial, after 400mg bd dose. Patient was very anxious and the perceived intoxicating effects of IMP may have been due to psychosomatic concerns		
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Psychosis			

subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 March 2014	1) An additional secondary objective: "To determine whether measures of brain activity using magnetic resonance imaging can predict response to CBD, and whether these measures change with response to CBD" 2) The addition of the following endpoints: "Brain glutamate measures with 1H-MRS, blood flow using ASL and BOLD response with fMRI imaging methods" 3) A modification to the following inclusion criteria: Aged 18-6035 (inclusive) meeting DSM IV criteria for schizophrenia within the first 3 years of presentation to psychiatric services. 4) An update to the Investigator Brochure (Edition 6 August 2013) in the form of a Development Core Safety Information (DSCI) detailing a revision to section 7.6 (Safety), which will be included as appendix 3 to the current IB.
27 March 2015	The amendment consists of the removal of one of the exclusion criteria. It is expected this will result in an increase in patient recruitment, and an, albeit slight, change in patient population studied, and is therefore deemed as a substantial amendment for the MHRA. The following criteria was removed; Concomitant anti-depressant/anti-convulsant treatment for 2-months prior to study entry.

Notes:

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.

July 2015 the IMP expired. The IMP was sent for analysis and was found to be unstable so a shelf-life so a shelf-life
extension was not granted. Additionally the Science had moved on by this stage. Insufficient data had been obtained for analysis.

Notes: