Clinical trial results:
A Randomised, Partially-blind, Placebo-controlled, Pilot, Dose-ranging Study To Assess The Effect Of Cannabidiol (CBD) On Liver Fat Levels In Subjects With Fatty Liver Disease.

Summary

EudraCT number	2009-017080-41
Trial protocol	GB
Global end of trial date	13 July 2012

Results information

Result version number	v1 (current)
This version publication date	03 October 2018
First version publication date	03 October 2018

Trial information

Trial identification

Sponsor protocol code	GWMD09112

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01284634
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GW Research Ltd
Sponsor organisation address	Sovereign House, Vision Park, Chivers Way, Histon, Cambridge, United Kingdom, CB24 9BZ
Public contact	Alternate contact: medinfo@greenwichbiosciences.com, GW Research Ltd, medinfo@gwpharm.com
Scientific contact	Alternate contact: medinfo@greenwichbiosciences.com, GW Research Ltd, medinfo@gwpharm.com

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 November 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 July 2012
Global end of trial reached?	Yes
Global end of trial date	13 July 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of GWP42003 on liver triglyceride levels (liver fat) in participants with fatty liver disease (FLD).

Protection of trial subjects:

This study was conducted in accordance with International Council on Harmonisation Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted. No study procedures were performed on study candidates until written consent had been obtained from the participant. The informed consent form, protocol, and amendments for this study were submitted to and approved by an independent ethics committee.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	03 May 2011
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: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	22
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants had been clinically diagnosed with FLD, and had liver fat levels ≥5% as measured by Magnetic Resonance Imaging/ Magnetic Resonance Scanning (MRI/MRS) scanning, or a biopsy within two months prior to screening.

Period 1

Period 1 title	Baseline, Treatment, and Follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

This study was partially-blinded. Due to the varying numbers of capsules to be administered, participants and investigators were not blinded to the treatment cohort (one, two or four capsules), but were blinded to the treatment allocation within each cohort (GWP42003 200, 400, or 800 milligrams [mg] or placebo).

Arms

Are arms mutually exclusive?	Yes
Arm title	GWP42003 200 mg/Day Dose

Arm description:

Participants self-administered one 100 mg GWP42003 capsule twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).

Arm type	Experimental
Investigational medicinal product name	GWP42003
Investigational medicinal product code	
Other name	Cannabidiol, CBD
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GWP42003 was presented as Licaps® size double zero (Size 00) hard gelatin capsules containing 100 mg of CBD dissolved in vehicle (Gelucire 44/14).

Arm title	GWP42003 400 mg/Day Dose

Arm description:

Participants self-administered two x 100 mg GWP42003 capsules twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).

Arm type	Experimental
Investigational medicinal product name	GWP42003
Investigational medicinal product code	
Other name	Cannabidiol, CBD
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GWP42003 was presented as Licaps® size double zero (Size 00) hard gelatin capsules containing 100 mg of CBD dissolved in vehicle (Gelucire 44/14).

Arm title	GWP42003 800 mg/Day Dose

Arm description:

Participants self-administered four x 100 mg GWP42003 capsules twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).

Arm type	Experimental
Investigational medicinal product name	GWP42003
Investigational medicinal product code	
Other name	Cannabidiol, CBD
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GWP42003 was presented as Licaps® size double zero (Size 00) hard gelatin capsules containing 100 mg of CBD dissolved in vehicle (Gelucire 44/14).

Arm title	Placebo

Arm description:

Participants self-administered one, two or four placebo capsules twice daily, for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).

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

Dosage and administration details:

Placebo was presented as Licaps® size double zero (Size 00) hard gelatin capsules containing excipients (Gelucire 44/14).

Number of subjects in period 1	GWP42003 200 mg/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose
Started	7	6	7
Received at least 1 dose of study drug	7	6	7
Intent to Treat Analysis Set	7	6	7
Safety Analysis Set	7	6	7
Completed	6	6	5
Not completed	1	0	2
Adverse event, non-fatal	1	-	2

Number of subjects in period 1	Placebo
Started	5
Received at least 1 dose of study drug	5
Intent to Treat Analysis Set	5
Safety Analysis Set	5
Completed	4
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	GWP42003 200 mg/Day Dose
Reporting group description:	
Participants self-administered one 100 mg GWP42003 capsule twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).	
Reporting group title	GWP42003 400 mg/Day Dose
Reporting group description:	
Participants self-administered two x 100 mg GWP42003 capsules twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).	
Reporting group title	GWP42003 800 mg/Day Dose
Reporting group description:	
Participants self-administered four x 100 mg GWP42003 capsules twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).	
Reporting group title	Placebo
Reporting group description:	
Participants self-administered one, two or four placebo capsules twice daily, for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).	

Reporting group values	GWP42003 200 mg/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose
Number of subjects	7	6	7
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	40.69	49.08	46.90
standard deviation	± 14.62	± 7.72	± 12.57
Gender categorical			
Units: Subjects			
Female	5	2	2
Male	2	4	5

Reporting group values	Placebo	Total	
Number of subjects	5	25	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	50.41		
standard deviation	± 18.41	-	
Gender categorical			
Units: Subjects			
Female	4	13	

Male	1	12	

End points

End points reporting groups

Reporting group title	GWP42003 200 mg/Day Dose
Reporting group description:	
Participants self-administered one 100 mg GWP42003 capsule twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).	
Reporting group title	GWP42003 400 mg/Day Dose
Reporting group description:	
Participants self-administered two x 100 mg GWP42003 capsules twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).	
Reporting group title	GWP42003 800 mg/Day Dose
Reporting group description:	
Participants self-administered four x 100 mg GWP42003 capsules twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).	
Reporting group title	Placebo
Reporting group description:	
Participants self-administered one, two or four placebo capsules twice daily, for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).	

Primary: Percent Change From Baseline To The End Of Treatment (EOT) In Mean Liver Triglyceride Levels

End point title	Percent Change From Baseline To The End Of Treatment (EOT) In Mean Liver Triglyceride Levels
End point description:	
Liver triglyceride levels were measured by MRI/MRS scanning and the percent change from baseline to the EOT in group mean levels was investigated. A reduction from baseline, that is, a negative value, indicates an improvement in condition.	
End point type	Primary
End point timeframe:	
Baseline to EOT (Day 57) or Early Termination (ET)	

End point values	GWP42003 200 mg/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	5
Units: percent change				
arithmetic mean (standard deviation)	-0.68 (± 4.97)	-0.28 (± 8.60)	0.65 (± 5.28)	6.36 (± 17.97)

Statistical analyses

Statistical analysis title	% Change From BL In Mean Liver Triglyceride Levels

Statistical analysis description:

All participants who were randomized, received at least one dose of study medication and had on-treatment efficacy data were included in the ITT analysis set. The EOT liver triglyceride levels were analysed using a linear regression model, with EOT triglyceride levels as the dependent variable, dose of GWP42003 as regressor, baseline liver triglyceride levels as a covariate, and gender as a factor.

Comparison groups	GWP42003 200 mg/Day Dose v Placebo
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.222
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-6.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	-16.35
upper limit	2.56
Variability estimate	Standard error of the mean
Dispersion value	5.454

Statistical analysis title	% Change from BL In Mean Liver Triglyceride Levels

Statistical analysis description:

All participants who were randomized, received at least one dose of study medication and had on-treatment efficacy data were included in the ITT analysis set. The EOT liver triglyceride levels were analysed using a linear regression model, with EOT triglyceride levels as the dependent variable, dose of GWP42003 as regressor, baseline liver triglyceride levels as a covariate, and gender as a factor.

Comparison groups	GWP42003 400 mg/Day Dose v Placebo
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.133
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-9.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	-19.66
upper limit	0.95
Variability estimate	Standard error of the mean
Dispersion value	5.943

Statistical analysis title	% Change From BL In Mean Liver Triglyceride Levels

Statistical analysis description:

All participants who were randomized, received at least one dose of study medication and had on-treatment efficacy data were included in the ITT analysis set. The EOT liver triglyceride levels were analysed using a linear regression model, with EOT triglyceride levels as the dependent variable, dose of GWP42003 as regressor, baseline liver triglyceride levels as a covariate, and gender as a factor.

Comparison groups	GWP42003 800 mg/Day Dose v Placebo
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.302
Method	Regression, Linear
Parameter estimate	Median difference (final values)
Point estimate	-6.54
Confidence interval	
level	90 %
sides	2-sided
lower limit	-17.22
upper limit	4.14
Variability estimate	Standard error of the mean
Dispersion value	6.158

Secondary: Change From Baseline To The EOT In Mean Serum Total Cholesterol Levels

End point title	Change From Baseline To The EOT In Mean Serum Total Cholesterol Levels

End point description:

A fasting blood sample was taken for the measurement of serum total cholesterol. A reduction from baseline, that is, a negative value, indicates an improvement in condition.

End point type	Secondary

End point timeframe:

Baseline to EOT (Day 57) or ET

End point values	GWP42003 200 mg/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	7	5
Units: Millimole (mmol)/Litre (L)				
arithmetic mean (standard deviation)	0.07 (± 0.76)	0.03 (± 0.51)	-0.14 (± 0.31)	-0.62 (± 1.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The EOT In Mean Serum High Density Lipoprotein (HDL)-Cholesterol (C) Levels

End point title	Change From Baseline To The EOT In Mean Serum High Density Lipoprotein (HDL)-Cholesterol (C) Levels

End point description:

A fasting blood sample was obtained for the measurement of HDL-C. An increase from baseline, that is, a positive value, indicates an improvement in condition.

End point type	Secondary

End point timeframe:

Baseline to EOT (Day 57) or ET

End point values	GWP42003 200 mg/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	7	5
Units: mmol/L				
arithmetic mean (standard deviation)	0.07 (± 0.15)	0.08 (± 0.15)	0.06 (± 0.17)	-0.14 (± 0.23)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The EOT In Mean Serum HDL: Low Density Lipoprotein (LDL)-C Ratio

End point title	Change From Baseline To The EOT In Mean Serum HDL: Low Density Lipoprotein (LDL)-C Ratio

End point description:

A fasting blood sample was obtained for the measurement of HDL-C and LDL-C, allowing the HDL:LDL cholesterol ratio to be calculated. An increase from baseline, that is, a positive value, indicates an improvement in condition.

End point type	Secondary

End point timeframe:

Baseline to EOT (Day 57) or ET

End point values	GWP42003 200 mg/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	7	5
Units: change in ratio				
arithmetic mean (standard deviation)	-0.02 (± 0.13)	-0.00 (± 0.08)	0.03 (± 0.09)	0.01 (± 0.06)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The EOT In Mean Serum Triglyceride Levels

End point title	Change From Baseline To The EOT In Mean Serum Triglyceride Levels

End point description:

A fasting blood sample was obtained for the measurement of serum triglycerides. A reduction from baseline, that is, a negative value, indicates an improvement in condition.

End point type	Secondary

End point timeframe:

Baseline to EOT (Day 57) or ET

End point values	GWP42003 200 mg/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	7	5
Units: mmol/L				
arithmetic mean (standard deviation)	-0.40 (± 1.05)	-0.29 (± 0.82)	-0.50 (± 1.16)	-0.28 (± 0.39)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The EOT In Mean Serum LDL-C Levels

End point title	Change From Baseline To The EOT In Mean Serum LDL-C Levels

End point description:

A fasting blood sample was obtained for the measurement of LDL-C. An increase from baseline, that is, a positive value, indicates an improvement in condition.

End point type	Secondary

End point timeframe:

Baseline to EOT (Day 57) or ET

End point values	GWP42003 200 mg/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	7	5
Units: mmol/l				
arithmetic mean (standard deviation)	0.11 (± 0.631)	0.08 (± 0.407)	0.00 (± 0.432)	-0.34 (± 0.737)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 through Day 77 (Safety Follow-up)

Adverse event reporting additional description:

Safety analysis set: All correctly randomized participants who received at least one dose of IMP were included and analyzed according to the treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	GWP42003 200 milligrams (mg)/Day Dose

Reporting group description:

Participants self-administered one x 100 mg GWP42003 capsule twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).

Reporting group title	GWP42003 400 mg/Day Dose

Reporting group description:

Participants self-administered two x 100 mg GWP42003 capsules twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).

Reporting group title	GWP42003 800 mg/Day Dose

Reporting group description:

Participants self-administered four x 100 mg GWP42003 capsules twice daily for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).

Reporting group title	Placebo

Reporting group description:

Participants self-administered one, two or four placebo capsules twice daily, for 8 weeks (the first dose was 30 minutes before breakfast [fasted] and the second was 30 minutes before the evening meal [typically 12 hours apart]).

Serious adverse events	GWP42003 200 milligrams (mg)/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo		
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: 5 %

Non-serious adverse events	GWP42003 200 milligrams (mg)/Day Dose	GWP42003 400 mg/Day Dose	GWP42003 800 mg/Day Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	5 / 6 (83.33%)	7 / 7 (100.00%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Product size issue			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			

Depressed mood			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Heart sounds abnormal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	1 / 7 (14.29%)	3 / 6 (50.00%)	2 / 7 (28.57%)
occurrences (all)	2	3	2
Lethargy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Poor quality sleep			

subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Meniere's disease			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Abnormal faeces			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Change of bowel habit			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Defaecation urgency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	4 / 7 (57.14%)	3 / 6 (50.00%)	5 / 7 (71.43%)
occurrences (all)	5	6	8
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	2
Eructation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Flatulence			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal hypermotility			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	3	0	1
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Rash generalised			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Pollakiuria			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Product size issue			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Heart sounds abnormal			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Poor quality sleep			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Meniere's disease			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			

Abdominal distension subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1			
Abdominal pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 2			
Abnormal faeces subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1			
Change of bowel habit subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1			
Defaecation urgency subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0			
Diarrhoea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0			
Dyspepsia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0			
Eructation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0			
Flatulence subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1			
Frequent bowel movements subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0			
Gastritis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0			
Gastrointestinal hypermotility subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0			

Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 0 / 5 (0.00%) 0 1 / 5 (20.00%) 1		
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash generalised subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	 0 / 5 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all)	 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0		

Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Tooth abscess			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Tooth infection			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 5 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2010	The protocol was updated to include use of MRI/MRS scanning in the study. Urine tetrahydrocannabinol testing procedures were also added.
17 May 2011	The screening period was increased to allow MRI/MRS scanning to determine eligibility of participants. One additional withdrawal criterion and flexibility on visit windows was introduced. Typographical errors were corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported