Clinical trial results:
A randomised, double-blind, placebo-controlled parallel group, pilot study of GWP42003 in the symptomatic treatment of ulcerative colitis.

Summary

EudraCT number	2011-003208-19
Trial protocol	GB CZ
Global end of trial date	05 August 2014

Results information

Result version number	v1 (current)
This version publication date	23 September 2018
First version publication date	23 September 2018

Trial information

Trial identification

Sponsor protocol code	GWID10160

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01562314
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	30 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 August 2014
Global end of trial reached?	Yes
Global end of trial date	05 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of GWP42003 compared with placebo by the percentage of participants achieving remission quantified as a MAYO score of 2 or less (with no sub-score >1) after 10 weeks treatment.

Protection of trial subjects:

This study was conducted in accordance with International Conference 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 the institutional review board or independent ethics committee at each participating study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2012
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: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	56
From 65 to 84 years	4

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were screened for eligibility over a period of 7 days.

Period 1

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

Blinding implementation details:

To maintain blinding throughout, all capsule medication was formulated in such a way as to disguise the appearance, smell and taste of the active materials by the use of identical excipients and capsule shells. The maximum number of dose units administered was identical in both treatment groups.

Arms

Are arms mutually exclusive?	Yes
Arm title	GWP42003

Arm description:

GWP42003 was administered orally at a dose of 50 milligrams (mg) up to 250 mg, twice daily (BID), in the fasted state in the morning and evening, for 10 weeks. Following randomization, participants entered a 2-week dose escalation period to achieve their maximum tolerated dose, up to 500 mg, and maintained this dose for the rest of the treatment period. Participants were then followed for 1 week.

Arm type	Experimental
Investigational medicinal product name	GWP42003
Investigational medicinal product code	GWP42003
Other name	Cannabidiol (CBD), Botanical Drug Substance (BDS)
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 to 5 50 mg capsules taken BID

Arm title	Placebo

Arm description:

Placebo capsules matching the study drug were administered orally, BID, in the fasted state in the morning and evening, for 10 weeks. Participants were then followed for 1 week.

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

Dosage and administration details:

1 to 5 matching capsules taken BID

Number of subjects in period 1	GWP42003	Placebo
Started	29	31
Received at least 1 dose of study drug	29	31
Intent-to-Treat (ITT) Analysis Set	29	31
Safety Analysis Set	29	31
Per Protocol (PP) Analysis Set	17	27
Completed	16	23
Not completed	13	8
Adverse Event	10	5
Withdrawal by Subject	-	1
Met Withdrawal Criteria	3	2

Baseline characteristics

Reporting groups	
Reporting group title	GWP42003
Reporting group description:	
GWP42003 was administered orally at a dose of 50 milligrams (mg) up to 250 mg, twice daily (BID), in the fasted state in the morning and evening, for 10 weeks. Following randomization, participants entered a 2-week dose escalation period to achieve their maximum tolerated dose, up to 500 mg, and maintained this dose for the rest of the treatment period. Participants were then followed for 1 week.	
Reporting group title	Placebo
Reporting group description:	
Placebo capsules matching the study drug were administered orally, BID, in the fasted state in the morning and evening, for 10 weeks. Participants were then followed for 1 week.	

Reporting group values	GWP42003	Placebo	Total
Number of subjects	29	31	60
Age categorical Units: Subjects			
18-64 years	26	30	56
65-84 years	3	1	4
Age continuous Units: years			
arithmetic mean	44.78	42.82	
standard deviation	± 15.050	± 12.916	-
Gender categorical Units: Subjects			
Female	6	10	16
Male	23	21	44

End points

End points reporting groups

Reporting group title	GWP42003

Reporting group description:

GWP42003 was administered orally at a dose of 50 milligrams (mg) up to 250 mg, twice daily (BID), in the fasted state in the morning and evening, for 10 weeks. Following randomization, participants entered a 2-week dose escalation period to achieve their maximum tolerated dose, up to 500 mg, and maintained this dose for the rest of the treatment period. Participants were then followed for 1 week.

Reporting group title	Placebo

Reporting group description:

Placebo capsules matching the study drug were administered orally, BID, in the fasted state in the morning and evening, for 10 weeks. Participants were then followed for 1 week.

Subject analysis set title	GWP42003 - ITT Analysis Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All participants who were randomized and received at least 1 dose of study drug. Participants were analyzed according to the group to which they were randomized.

Subject analysis set title	Placebo - ITT Analysis Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All participants who were randomized and received at least 1 dose of study drug. Participants were analyzed according to the group to which they were randomized.

Subject analysis set title	GWP42003 - PP Analysis Set
Subject analysis set type	Per protocol

Subject analysis set description:

All participants without protocol violations that compromised the assessments of efficacy.

Subject analysis set title	Placebo - PP Analysis Set
Subject analysis set type	Per protocol

Subject analysis set description:

All participants without protocol violations that compromised the assessments of efficacy.

Primary: Number Of Participants With A Mayo Score Of 2 Or Less (With No Sub-score >1) At EOT

End point title	Number Of Participants With A Mayo Score Of 2 Or Less (With No Sub-score >1) At EOT

End point description:

The Mayo score is an assessment of ulcerative colitis activity. The Mayo total score ranges from 0 to 12 points with higher scores indicating more severe disease. The total score is made up of 4 sub-scores, each of which is assessed using a 0 to 3 scale. Sub-scores are graded as follows: Stool Frequency: 0 = Normal number of stools, 1 = 1 to 2 stools more than normal, 2 = 3 to 4 stools more than normal, 3 = 5 or more stools more than normal; Rectal Bleeding: 0 = No blood seen, 1 = Streaks of blood with stool less than half the time, 2 = Obvious blood with stool most of the time or more, 3 = Blood alone passes; Findings on Endoscopy: 0 = Normal or inactive disease, 1 = Mild disease (erythema, decreased vascular pattern, mild friability), 2 = Moderate disease (marked erythema, lack of vascular pattern, friability, erosions), 3 = Severe disease (spontaneous bleeding, ulceration); PGAS: 0 = none, 1 = mild, 2 = moderate, and 3 = severe.

End point type	Primary

End point timeframe:

Baseline to End of Treatment (EOT) (10 weeks) or Early Termination (ET)

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	31		
Units: count of participants	8	8		

Statistical analyses

Statistical analysis title	Mayo Score Of 2 Or Less - ITT Analysis Set
Comparison groups	GWP42003 - ITT Analysis Set v Placebo - ITT Analysis Set
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7532
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.821
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.292
upper limit	2.309

Primary: Number Of Participants With A Mayo Score Of 2 Or Less (With No Sub-score >1) At EOT - PP Analysis Set

End point title	Number Of Participants With A Mayo Score Of 2 Or Less (With No Sub-score >1) At EOT - PP Analysis Set

End point description:

The Mayo score is an assessment of ulcerative colitis activity. The Mayo total score ranges from 0 to 12 points with higher scores indicating more severe disease. The total score is made up of 4 sub-scores, each of which is assessed using a 0 to 3 scale. Sub-scores are graded as follows: Stool Frequency: 0 = Normal number of stools, 1 = 1 to 2 stools more than normal, 2 = 3 to 4 stools more than normal, 3 = 5 or more stools more than normal; Rectal Bleeding: 0 = No blood seen, 1 = Streaks of blood with stool less than half the time, 2 = Obvious blood with stool most of the time or more, 3 = Blood alone passes; Findings on Endoscopy: 0 = Normal or inactive disease, 1 = Mild disease (erythema, decreased vascular pattern, mild friability), 2 = Moderate disease (marked erythema, lack of vascular pattern, friability, erosions), 3 = Severe disease (spontaneous bleeding, ulceration); PGAS: 0 = none, 1 = mild, 2 = moderate, and 3 = severe.

End point type	Primary

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: count of participants	7	8		

Statistical analyses

Statistical analysis title	Mayo Score Of 2 Or Less - PP Analysis Set
Comparison groups	Placebo - PP Analysis Set v GWP42003 - PP Analysis Set
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7032
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.419
upper limit	4.04

Secondary: Distribution On The PGAS At EOT

End point title	Distribution On The PGAS At EOT
End point description:	
The PGAS required the physician to assess participants' disease severity on a 4-point scale (0 = normal [no disease], 1 = mild disease, 2 = moderate disease, 3 = severe disease).	
End point type	Secondary
End point timeframe:	
EOT (10 weeks) or ET	

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	31		
Units: count of participants				
Normal	7	5		
Mild Disease	13	11		
Moderate Disease	6	12		
Severe Disease	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Distribution On The PGAS At EOT - PP Analysis

End point title	Distribution On The PGAS At EOT - PP Analysis

End point description:

The PGAS required the physician to assess participants' disease severity on a 4-point scale (0 = normal [no disease], 1 = mild disease, 2 = moderate disease, 3 = severe disease).

End point type	Secondary

End point timeframe:

EOT (10 weeks) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: count of participants				
Normal	6	5		
Mild Disease	8	9		
Moderate Disease	3	11		
Severe Disease	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To EOT In The PGAS Score

End point title	Change From Baseline To EOT In The PGAS Score

End point description:

The PGAS required the physician to assess participants' disease severity on a 4-point scale (0 = normal [no disease], 1 = mild disease, 2 = moderate disease, 3 = severe disease). A negative change from Baseline indicates that symptoms decreased.

End point type	Secondary

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	31		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	1.7 (± 0.45)	1.8 (± 0.48)		
Final Visit	1.0 (± 0.72)	1.4 (± 0.89)		
Change From Baseline	-0.8 (± 0.82)	-0.4 (± 0.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To EOT In The PGAS Score - PP Analysis

End point title	Change From Baseline To EOT In The PGAS Score - PP Analysis

End point description:

The PGAS required the physician to assess participants' disease severity on a 4-point scale (0 = normal [no disease], 1 = mild disease, 2 = moderate disease, 3 = severe disease). A negative change from Baseline indicates that symptoms decreased.

End point type	Secondary

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	1.8 (± 0.44)	1.8 (± 0.51)		
Final Visit	0.8 (± 0.73)	1.4 (± 0.88)		
Change From Baseline	-0.9 (± 0.83)	-0.4 (± 0.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To EOT In The Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score

End point title	Change From Baseline To EOT In The Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score

End point description:

The IBDQ is a validated and reliable tool to measure health-related quality of life in adult participants with inflammatory bowel disease (IBD). Each of the 32 questions falls into 1 of 4 domains (bowel

symptoms, systemic symptoms, emotional status, and social function). The 32 questions each have 7 possible responses. Each response is assigned a score ranging from 1 to 7, indicating the severity (1 being least favorable and 7 being the most favorable). Individual question scores were summed to give the IBDQ total score (range: 32 to 224 points). A positive change from Baseline indicates that symptoms improved.

End point type	Secondary

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	31		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	138.5 (± 32.37)	129.1 (± 38.02)		
Final Visit	164.2 (± 29.13)	146.8 (± 47.50)		
Change From Baseline	24.6 (± 35.51)	16.7 (± 36.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To EOT In The IBDQ Total Score - PP Analysis

End point title	Change From Baseline To EOT In The IBDQ Total Score - PP Analysis

End point description:

The IBDQ is a validated and reliable tool to measure health-related quality of life in adult participants with IBD. Each of the 32 questions falls into 1 of 4 domains (bowel symptoms, systemic symptoms, emotional status, and social function). The 32 questions each have 7 possible responses. Each response is assigned a score ranging from 1 to 7, indicating the severity (1 being least favorable and 7 being the most favorable). Individual question scores were summed to give the IBDQ total score (range: 32 to 224 points). A positive change from Baseline indicates that symptoms improved.

End point type	Secondary

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	134.0 (± 35.58)	134.0 (± 37.30)		

Final Visit	172.8 (± 28.52)	150.5 (± 48.87)		
Change From Baseline	39.3 (± 39.81)	15.4 (± 33.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number Of Participants Who Reported An Improvement In The Subject Global Impression Of Change (SGIC) Questionnaire At EOT

End point title	Number Of Participants Who Reported An Improvement In The Subject Global Impression Of Change (SGIC) Questionnaire At EOT

End point description:

Participants were asked to answer the following question by using a 7-point scale (1 = very much better to 7 = very much worse): "Please assess the change in your ulcerative colitis symptoms since immediately before receiving the first dose of study treatment." Improvement was considered as very much better, much better, or minimally better.

End point type	Secondary

End point timeframe:

Visit 4 (Day 43) to EOT (10 weeks) or ET

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	31		
Units: count of participants				
Visit 4 (Day 43)	15	18		
Final Visit	23	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number Of Participants Who Reported An Improvement In The SGIC Questionnaire At EOT - PP Analysis

End point title	Number Of Participants Who Reported An Improvement In The SGIC Questionnaire At EOT - PP Analysis

End point description:

Participants were asked to answer the following question by using a 7-point scale (1 = very much better to 7 = very much worse): "Please assess the change in your ulcerative colitis symptoms since immediately before receiving the first dose of study treatment." Improvement was considered as very much better, much better, or minimally better.

End point type	Secondary

End point timeframe:

Visit 4 (Day 43) to EOT (10 weeks) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: count of participants				
Visit 4 (Day 43)	14	18		
Final Visit	16	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The Last Week Of Treatment In Ulcerative Colitis Symptoms, As Measured By Scores On The Stool Frequency Numerical Rating Scale (NRS)

End point title	Change From Baseline To The Last Week Of Treatment In Ulcerative Colitis Symptoms, As Measured By Scores On The Stool Frequency Numerical Rating Scale (NRS)

End point description:

Participants were required to record their stool frequency during the baseline and treatment periods in a daily diary. Participants graded stool frequency with a 4-point NRS as follows: 0 = Normal number of stools; 1 = 1 to 2 stools more than normal; 2 = 3 to 4 stools more than normal; 3 = 5 or more stools more than normal. For analysis, the baseline value was defined as the mean stool frequency score of the last 7 available days of the baseline period; the EOT value was defined as the mean stool frequency score of last 7 days of the treatment period, or last 7 days for which study drug was taken, where earlier. A negative change from Baseline indicates that symptoms improved.

End point type	Secondary

End point timeframe:

Baseline to EOT (last 7 days) or ET

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	31		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	1.50 (± 0.937)	1.89 (± 0.814)		
Last 7 Days	1.05 (± 0.930)	1.46 (± 0.888)		
Change From Baseline	-0.43 (± 0.563)	-0.43 (± 0.816)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The Last Week Of Treatment In Ulcerative Colitis Symptoms, As Measured By Scores On The Stool Frequency NRS - PP Analysis

End point title	Change From Baseline To The Last Week Of Treatment In Ulcerative Colitis Symptoms, As Measured By Scores On The Stool Frequency NRS - PP Analysis

End point description:

Participants were required to record their stool frequency during the baseline and treatment periods in a daily diary. Participants graded stool frequency with a 4-point NRS as follows: 0 = Normal number of stools; 1 = 1 to 2 stools more than normal; 2 = 3 to 4 stools more than normal; 3 = 5 or more stools more than normal. For analysis, the baseline value was defined as the mean stool frequency score of the last 7 available days of the baseline period; the EOT value was defined as the mean stool frequency score of last 7 days of the treatment period, or last 7 days for which study drug was taken, where earlier. A negative change from Baseline indicates that symptoms improved.

End point type	Secondary

End point timeframe:

Baseline to EOT (last 7 days) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	1.37 (± 0.875)	1.81 (± 0.827)		
Last 7 Days	0.73 (± 0.689)	1.36 (± 0.871)		
Change From Baseline	-0.64 (± 0.497)	-0.45 (± 0.768)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The Last Week Of Treatment In Ulcerative Colitis Symptoms, As Measured By Scores On The Rectal Bleeding NRS

End point title	Change From Baseline To The Last Week Of Treatment In Ulcerative Colitis Symptoms, As Measured By Scores On The Rectal Bleeding NRS

End point description:

Participants were required to record their rectal bleeding during the baseline and treatment periods in a daily diary. Participants graded rectal bleeding with a 4-point NRS as follows: 0 = No blood seen, 1 = Streaks of blood with stool less than half the time, 2 = Obvious blood with stool most of the time or more, 3 = Blood alone passes. For analysis, the baseline value was defined as the mean rectal bleeding score of the last 7 available days of the baseline period; the EOT value was defined as the mean rectal bleeding score of last 7 days of the treatment period, or last 7 days for which study drug was taken, where earlier. A negative change from Baseline indicates that symptoms improved.

End point type	Secondary

End point timeframe:

Baseline to EOT (last 7 days) or ET

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	31		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	0.96 (± 0.829)	1.19 (± 0.816)		
Last 7 Days	0.48 (± 0.711)	0.84 (± 0.863)		
Change From Baseline	-0.44 (± 0.709)	-0.35 (± 0.794)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The Last Week Of Treatment In Ulcerative Colitis Symptoms, As Measured By Scores On The Rectal Bleeding NRS - PP Analysis

End point title	Change From Baseline To The Last Week Of Treatment In Ulcerative Colitis Symptoms, As Measured By Scores On The Rectal Bleeding NRS - PP Analysis

End point description:

Participants were required to record their rectal bleeding during the baseline and treatment periods in a daily diary. Participants graded rectal bleeding with a 4-point NRS as follows: 0 = No blood seen, 1 = Streaks of blood with stool less than half the time, 2 = Obvious blood with stool most of the time or more, 3 = Blood alone passes. For analysis, the baseline value was defined as the mean rectal bleeding score of the last 7 available days of the baseline period; the EOT value was defined as the mean rectal bleeding score of last 7 days of the treatment period, or last 7 days for which study drug was taken, where earlier. A negative change from Baseline indicates that symptoms improved.

End point type	Secondary

End point timeframe:

Baseline to EOT (last 7 days) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	0.82 (± 0.682)	1.16 (± 0.831)		
Last 7 Days	0.24 (± 0.367)	0.80 (± 0.875)		
Change From Baseline	-0.58 (± 0.793)	-0.35 (± 0.773)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To EOT In The Mayo Total Score

End point title	Change From Baseline To EOT In The Mayo Total Score

End point description:

The Mayo score is an assessment of ulcerative colitis activity. The Mayo total score ranges from 0 to 12 points with higher scores indicating more severe disease. The total score is made up of 4 sub-scores (assessed using a 0 to 3 scale). The sub-scores are graded as follows: Stool Frequency: 0 = Normal number of stools, 1 = 1 to 2 stools more than normal, 2 = 3 to 4 stools more than normal, 3 = 5 or more stools more than normal; Rectal Bleeding: 0 = No blood seen, 1 = Streaks of blood with stool less than half the time, 2 = Obvious blood with stool most of the time or more, 3 = Blood alone passes; Findings on Endoscopy: 0 = Normal or inactive disease, 1 = Mild disease (erythema, decreased vascular pattern, mild friability), 2 = Moderate disease (marked erythema, lack of vascular pattern, friability, erosions), 3 = Severe disease (spontaneous bleeding, ulceration); PGAS: 0 = none, 1 = mild, 2 = moderate, and 3 = severe. A negative change from Baseline indicates that symptoms improved.

End point type	Secondary

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	31		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	6.3 (± 1.73)	7.0 (± 2.01)		
Final Visit	3.0 (± 2.25)	4.9 (± 3.22)		
Change From Baseline	-3.0 (± 2.40)	-1.8 (± 2.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To EOT In The Mayo Partial Score

End point title	Change From Baseline To EOT In The Mayo Partial Score

End point description:

The Mayo score is an assessment of ulcerative colitis activity. The Mayo partial score does not include the endoscopy findings sub-score and ranges from 0 to 9 points with higher scores indicating more severe disease. The partial score is made up of 3 sub-scores (assessed by using a 0 to 3 scale). The sub-scores are graded as follows: Stool Frequency: 0 = Normal number of stools, 1 = 1 to 2 stools more than normal, 2 = 3 to 4 stools more than normal, 3 = 5 or more stools more than normal; Rectal Bleeding: 0 = No blood seen, 1 = Streaks of blood with stool less than half the time, 2 = Obvious blood with stool most of the time or more, 3 = Blood alone passes; PGAS: 0 = none, 1 = mild, 2 = moderate, and 3 = severe. A negative change from Baseline indicates that symptoms improved.

End point type	Secondary

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	31		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	4.4 (± 1.57)	5.1 (± 1.61)		
Final Visit	2.3 (± 1.73)	3.8 (± 2.60)		
Change From Baseline	-2.0 (± 2.00)	-1.2 (± 2.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To EOT In Levels Of Fecal Calprotectin

End point title	Change From Baseline To EOT In Levels Of Fecal Calprotectin

End point description:

Fecal calprotectin is a marker of inflammation. Standard methods were used to measure the levels of calprotectin in fecal samples collected at the end of baseline and treatment periods. A negative change from Baseline indicates that levels of fecal calprotectin decreased.

End point type	Secondary

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - ITT Analysis Set	Placebo - ITT Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	31		
Units: microgram calprotectin/gram feces (ug/g)				
arithmetic mean (standard deviation)				
Baseline	490.6 (± 197.41)	462.3 (± 227.35)		
Final Visit	397.3 (± 241.08)	428.0 (± 229.38)		
Change From Baseline	-91.6 (± 295.77)	-51.3 (± 289.32)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Change From Baseline To EOT In The Mayo Total Score - PP Analysis

End point title	Change From Baseline To EOT In The Mayo Total Score - PP Analysis

End point description:

The Mayo score is an assessment of ulcerative colitis activity. The Mayo total score ranges from 0 to 12 points with higher scores indicating more severe disease. The total score is made up of 4 sub-scores (assessed using a 0 to 3 scale). The sub-scores are graded as follows: Stool Frequency: 0 = Normal number of stools, 1 = 1 to 2 stools more than normal, 2 = 3 to 4 stools more than normal, 3 = 5 or more stools more than normal; Rectal Bleeding: 0 = No blood seen, 1 = Streaks of blood with stool less than half the time, 2 = Obvious blood with stool most of the time or more, 3 = Blood alone passes; Findings on Endoscopy: 0 = Normal or inactive disease, 1 = Mild disease (erythema, decreased vascular pattern, mild friability), 2 = Moderate disease (marked erythema, lack of vascular pattern, friability, erosions), 3 = Severe disease (spontaneous bleeding, ulceration); PGAS: 0 = none, 1 = mild, 2 = moderate, and 3 = severe. A negative change from Baseline indicates that symptoms improved.

End point type	Post-hoc

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	6.0 (± 1.70)	6.8 (± 2.04)		
Final Visit	2.8 (± 2.02)	4.7 (± 3.24)		
Change From Baseline	-3.2 (± 2.25)	-1.9 (± 2.81)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Change From Baseline To EOT In The Mayo Partial Score - PP Analysis Set

End point title	Change From Baseline To EOT In The Mayo Partial Score - PP Analysis Set

End point description:

The Mayo score is an assessment of ulcerative colitis activity. The Mayo partial score does not include the endoscopy findings sub-score and ranges from 0 to 9 points with higher scores indicating more severe disease. The partial score is made up of 3 sub-scores (assessed by using a 0 to 3 scale). The sub-scores are graded as follows: Stool Frequency: 0 = Normal number of stools, 1 = 1 to 2 stools more than normal, 2 = 3 to 4 stools more than normal, 3 = 5 or more stools more than normal; Rectal Bleeding: 0 = No blood seen, 1 = Streaks of blood with stool less than half the time, 2 = Obvious blood with stool most of the time or more, 3 = Blood alone passes; PGAS: 0 = none, 1 = mild, 2 = moderate, and 3 = severe. A negative change from Baseline indicates that symptoms improved.

End point type	Post-hoc

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	4.1 (± 1.50)	4.9 (± 1.63)		
Final Visit	1.7 (± 1.53)	3.7 (± 2.66)		
Change From Baseline	-2.4 (± 2.03)	-1.2 (± 2.17)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Change From Baseline To EOT In Levels Of Fecal Calprotectin- PP Analysis

End point title	Change From Baseline To EOT In Levels Of Fecal Calprotectin- PP Analysis

End point description:

Fecal calprotectin is a marker of inflammation. Standard methods were used to measure the levels of calprotectin in fecal samples collected at the end of baseline and treatment periods. A negative change from Baseline indicates that levels of fecal calprotectin decreased.

End point type	Post-hoc

End point timeframe:

Baseline to EOT (10 weeks) or ET

End point values	GWP42003 - PP Analysis Set	Placebo - PP Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	27		
Units: ug/g				
arithmetic mean (standard deviation)				
Baseline	527.9 (± 164.14)	440.3 (± 237.99)		
Final Visit	355.9 (± 247.75)	408.9 (± 238.94)		
Change From Baseline	-155.9 (± 306.84)	-51.9 (± 311.56)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Post-dose on Day 1 through 14 days after the final dose (up to 85 days).

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	GWP42003

Reporting group description:

GWP42003 was administered orally at a dose of 50 mg up to 250 mg, BID, in the fasted state in the morning and evening, for 10 weeks. Following randomization, participants entered a 2-week dose escalation period to achieve their maximum tolerated dose, up to 500 mg, and maintained this dose for the rest of the treatment period. Participants were then followed for 1 week.

Reporting group title	Placebo

Reporting group description:

Placebo capsules matching the study drug were administered orally, BID, in the fasted state in the morning and evening, for 10 weeks. Participants were then followed for 1 week.

Serious adverse events	GWP42003	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	4 / 31 (12.90%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed[1]	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			

subjects affected / exposed	0 / 29 (0.00%)	2 / 31 (6.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This SAE affects only female participants.

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

Non-serious adverse events	GWP42003	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 29 (96.55%)	23 / 31 (74.19%)	
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 29 (6.90%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	5 / 29 (17.24%)	0 / 31 (0.00%)	
occurrences (all)	5	0	
Dizziness			
subjects affected / exposed	12 / 29 (41.38%)	3 / 31 (9.68%)	
occurrences (all)	13	3	
Headache			
subjects affected / exposed	4 / 29 (13.79%)	4 / 31 (12.90%)	
occurrences (all)	4	4	
Lethargy			
subjects affected / exposed	2 / 29 (6.90%)	2 / 31 (6.45%)	
occurrences (all)	2	2	
Memory impairment			
subjects affected / exposed	3 / 29 (10.34%)	0 / 31 (0.00%)	
occurrences (all)	3	0	
Somnolence			
subjects affected / exposed	10 / 29 (34.48%)	2 / 31 (6.45%)	
occurrences (all)	11	2	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	4 / 29 (13.79%)	4 / 31 (12.90%)	
occurrences (all)	5	4	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 29 (6.90%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Abdominal distension			
subjects affected / exposed	0 / 29 (0.00%)	3 / 31 (9.68%)	
occurrences (all)	0	3	
Abdominal pain			
subjects affected / exposed	1 / 29 (3.45%)	5 / 31 (16.13%)	
occurrences (all)	1	5	
Colitis			
subjects affected / exposed	1 / 29 (3.45%)	3 / 31 (9.68%)	
occurrences (all)	1	3	
Colitis ulcerative			
subjects affected / exposed	1 / 29 (3.45%)	3 / 31 (9.68%)	
occurrences (all)	1	3	
Constipation			
subjects affected / exposed	0 / 29 (0.00%)	3 / 31 (9.68%)	
occurrences (all)	0	3	
Dry mouth			
subjects affected / exposed	4 / 29 (13.79%)	0 / 31 (0.00%)	
occurrences (all)	5	0	
Nausea			
subjects affected / exposed	8 / 29 (27.59%)	3 / 31 (9.68%)	
occurrences (all)	8	3	
Vomiting			
subjects affected / exposed	4 / 29 (13.79%)	0 / 31 (0.00%)	
occurrences (all)	4	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 29 (0.00%)	3 / 31 (9.68%)	
occurrences (all)	0	3	
Psychiatric disorders			

Disorientation			
subjects affected / exposed	4 / 29 (13.79%)	0 / 31 (0.00%)	
occurrences (all)	4	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 29 (0.00%)	3 / 31 (9.68%)	
occurrences (all)	0	3	
Muscle twitching			
subjects affected / exposed	2 / 29 (6.90%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	3 / 29 (10.34%)	0 / 31 (0.00%)	
occurrences (all)	3	0	
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	2 / 29 (6.90%)	0 / 31 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2011	The amendment to this study updated contact details following GW Pharmaceuticals Ltd. office relocation.
24 June 2013	The amendment to this study amended the protocol to remove the lower dose limit of study drug. Topical treatments for ulcerative colitis within 2 weeks prior to screening were originally prohibited in the study protocol. This was changed so that participants on a stable dose of topical therapy for ulcerative colitis could be eligible in some circumstances. The amendment also divided the exclusion criterion 6.2.8 into 2 so that investigators could act at their discretion as to whether a participant with a history of significant psychiatric disorder or severe personality disorder was eligible for the study. Finally, the amendment resolved minor errors, inconsistencies and clarity issues.
21 August 2013	The amendment to this study further amendment the Prohibited Therapy section of the protocol to disallow topical treatments for ulcerative colitis within the last 2 weeks prior to the screening endoscopy. The amendment also included 3 minor administrative corrections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29538683