



Clinical trial results:

An exploratory, Phase 2, randomized, double-blind, placebo-controlled trial to investigate the safety and efficacy of cannabidiol oral solution (GWP42003-P; CBD-OS) in children and adolescents with Autism Spectrum Disorder.

Summary

EudraCT number	2020-002819-21
Trial protocol	DE ES
Global end of trial date	21 December 2023

Results information

Result version number	v1 (current)
This version publication date	07 July 2024
First version publication date	07 July 2024

Trial information

Trial identification

Sponsor protocol code	GWND19189
-----------------------	-----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04745026
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 150775

Notes:

Sponsors

Sponsor organisation name	Jazz Pharmaceuticals Research UK Limited
Sponsor organisation address	Building 730, Kent Science Park, Sittingbourne, Kent, United Kingdom, ME9 8AG
Public contact	Director Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals Research UK Limited, 1 215 8323750, ClinicalTrialDisclosure@JazzPharma.com
Scientific contact	Director of Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals Research UK Limited, 1 2158323750, ClinicalTrialDisclosure@JazzPharma.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	09 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 December 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of GWP42003-P in reducing symptom severity in children with Autism Spectrum Disorder (ASD).

Protection of trial subjects:

A copy of the protocol, proposed ICF, master ICF, other participant information material, any proposed advertising material, and any further documentation requested was submitted to the IRB/EC for written approval.

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki and the International Ethical Guidelines, applicable ICH GCP Guidelines, and other applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 May 2021
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	Spain: 4
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	United States: 67
Worldwide total number of subjects	103
EEA total number of subjects	4

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)	64
Adolescents (12-17 years)	39
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 191 patients were enrolled in the study. Of those 191 patients, 103 patients met all inclusion criteria and no exclusion criteria were randomized to treatment at 24 centers in the United States, Canada, Spain, United Kingdom, and Australia.

Pre-assignment

Screening details:

Eligible participants were randomized 7 to 14 days after the screening visit (Visit 1), once all required assessments were completed and laboratory results were reviewed. If required, screening assessments were permitted to be split over 2 visits; however, both visits were conducted within 7- to 14-day window prior to randomization (Visit 2).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GWP42003-P

Arm description:

Patients who were randomized to 5 mg/kg/day GWP42003-P for 1 week and then 10 mg/kg/day GWP42003-P for 11 weeks. At the end of treatment, participants tapered off the medication over a period of 1 week.

Arm type	Experimental
Investigational medicinal product name	GWP42003-P
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension in pre-filled oral applicator
Routes of administration	Oral use

Dosage and administration details:

Administered orally twice daily (morning and evening)

Arm title	Placebo
------------------	---------

Arm description:

Patients who were randomized to placebo for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension in pre-filled oral applicator
Routes of administration	Oral use

Dosage and administration details:

Administered twice daily (morning and evening)

Number of subjects in period 1	GWP42003-P	Placebo
Started	49	54
Completed	36	41
Not completed	13	13
Physician decision	1	-
Adverse event, non-fatal	2	2
Protocol violation	1	3
Lost to follow-up	4	3
Withdrawal by subject	5	5

Baseline characteristics

Reporting groups

Reporting group title	GWP42003-P
Reporting group description: Patients who were randomized to 5 mg/kg/day GWP42003-P for 1 week and then 10 mg/kg/day GWP42003-P for 11 weeks. At the end of treatment, participants tapered off the medication over a period of 1 week.	
Reporting group title	Placebo
Reporting group description: Patients who were randomized to placebo for 12 weeks.	

Reporting group values	GWP42003-P	Placebo	Total
Number of subjects	49	54	103
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	30	34	64
Adolescents (12-17 years)	19	20	39
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	11.1	10.8	-
standard deviation	± 3.02	± 3.01	-
Gender categorical			
Units: Subjects			
Female	13	7	20
Male	36	47	83
WASI-II Intelligent Quotient Score			
Units: score on a scale			
arithmetic mean	99.42	100.89	-
standard deviation	± 18.03	± 17.16	-
Aberrant Behavior Checklist Irritability			
GWP42003-P n=48; Placebo n=54			
Units: score on a scale			
arithmetic mean	23.2	22.5	-
standard deviation	± 7.36	± 8.74	-
Aberrant Behavior Checklist Social Withdrawal			
GWP42003-P n=48; Placebo n=54			
Units: score on a scale			
arithmetic mean	12.6	12.7	-
standard deviation	± 8.63	± 9.11	-

Aberrant Behavior Checklist Stereotypic Behavior			
GWP42003-P n=48; Placebo n=54			
Units: score on a scale			
arithmetic mean	6.7	6.7	
standard deviation	± 5.08	± 4.83	-
Aberrant Behavior Checklist Hyperactivity/Noncompliance			
GWP42003-P n=48; Placebo n=54			
Units: score on a scale			
arithmetic mean	25.2	26.9	
standard deviation	± 12.27	± 9.63	-
Aberrant Behavior Checklist Inappropriate Speech			
GWP42003-P n=48; Placebo n=54			
Units: score on a scale			
arithmetic mean	5.7	5.6	
standard deviation	± 3.22	± 3.08	-
Vineland Adaptive Behavior Scales Social and Communication Composite Score			
GWP42003-P n=48; Placebo n=50			
Units: score on a scale			
arithmetic mean	66.6	67.7	
standard deviation	± 19.61	± 15.18	-
Clinical Global Impression – Severity (CGI-S)			
GWP42003-P n=49; Placebo n=51			
Units: score on a scale			
arithmetic mean	4.76	4.82	
standard deviation	± 0.630	± 0.684	-

End points

End points reporting groups

Reporting group title	GWP42003-P
Reporting group description: Patients who were randomized to 5 mg/kg/day GWP42003-P for 1 week and then 10 mg/kg/day GWP42003-P for 11 weeks. At the end of treatment, participants tapered off the medication over a period of 1 week.	
Reporting group title	Placebo
Reporting group description: Patients who were randomized to placebo for 12 weeks.	

Primary: Change from Baseline in Aberrant Behavior Checklist (ABC) Subscale Total Scores

End point title	Change from Baseline in Aberrant Behavior Checklist (ABC) Subscale Total Scores
End point description: The caregiver-assessed ABC was designed to assess the presence and severity of various problem behaviors commonly observed in individuals diagnosed with intellectual and developmental disability. The checklist contains 5 subscales: Irritability (15 items); Social Withdrawal (16 items); Stereotypic Behavior (7 items); Hyperactivity/Noncompliance (16 items); and Inappropriate Speech (4 items). Each item is scored as 0 (never a problem), 1 (slight problem), 2 (moderately serious problem), or 3 (severe problem). The total score of all subscales ranges from 0 to 174 where higher scores indicate worse clinical outcome. The change from baseline to Week 4, Week 8, and Week 12 is reported with lower scores indicating better clinical outcome.	
End point type	Primary
End point timeframe: Baseline up to Week 12	

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49 ^[1]	54 ^[2]		
Units: score on a scale				
arithmetic mean (standard deviation)				
ABC-Irritability, Week 4	-6.35 (± 7.98)	-5.41 (± 7.16)		
ABC-Irritability, Week 8	-6.67 (± 8.63)	-8.05 (± 9.12)		
ABC-Irritability, Week 12	-6.97 (± 9.68)	-8.57 (± 10.10)		
ABC-Social Withdrawal, Week 4	-2.53 (± 5.61)	-2.92 (± 5.24)		
ABC-Social Withdrawal, Week 8	-3.81 (± 6.76)	-4.74 (± 6.25)		
ABC-Social Withdrawal, Week 12	-3.74 (± 6.21)	-4.51 (± 5.95)		
ABC-Stereotypic Behavior, Week 4	-2.10 (± 4.24)	-1.39 (± 3.24)		
ABC-Stereotypic Behavior, Week 8	-1.92 (± 3.99)	-1.98 (± 4.05)		
ABC-Stereotypic Behavior, Week 12	-1.88 (± 3.63)	-2.31 (± 4.03)		
ABC-Hyperactivity/Noncompliance, Week 4	-5.73 (± 8.08)	-4.55 (± 8.15)		
ABC-Hyperactivity/Noncompliance, Week 8	-6.39 (± 9.15)	-7.42 (± 9.06)		

ABC-Hyperactivity/Noncompliance, Week 12	-6.74 (\pm 10.62)	-8.77 (\pm 9.94)		
ABC-Inappropriate Speech, Week 4	-2.13 (\pm 2.88)	-0.88 (\pm 2.07)		
ABC-Inappropriate Speech, Week 8	-1.58 (\pm 2.74)	-1.44 (\pm 2.73)		
ABC-Inappropriate Speech, Week 12	-1.94 (\pm 2.93)	-1.51 (\pm 2.97)		

Notes:

[1] - All subscales

WK4:n=40; WK8: n=36; WK12:n=34

[2] - All subscales

WK4:n=51; WK8:n=43; WK12:n=35

Statistical analyses

Statistical analysis title	Irritability: GWP42003-P vs Placebo (Week 12)
Statistical analysis description:	
Superiority analysis	
Comparison groups	GWP42003-P v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.085 ^[3]
Method	Mixed models for repeated measures
Parameter estimate	Least square mean difference
Point estimate	3.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	7.21
Variability estimate	Standard error of the mean
Dispersion value	1.931

Notes:

[3] - Mixed models for repeated measures (MMRM) model includes randomization stratification factors, baseline score, visit, treatment arm, visit by treatment arm interaction as fixed effects, and visit repeated within each patient as a repeated effect.

Statistical analysis title	Social Withdrawal: GWP42003-P vs Placebo (Week 12)
Statistical analysis description:	
Superiority analysis	
Comparison groups	GWP42003-P v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3107 ^[4]
Method	Mixed models for repeated measures
Parameter estimate	Least square mean difference
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	3.36
Variability estimate	Standard error of the mean
Dispersion value	1.16

Notes:

[4] - Mixed models for repeated measures (MMRM) model includes randomization stratification factors, baseline score, visit, treatment arm, visit by treatment arm interaction as fixed effects, and visit repeated within each patient as a repeated effect.

Statistical analysis title	Stereotypic Behavior: GWP42003-P vs Placebo (WK12)
Statistical analysis description:	
Superiority analysis	
Comparison groups	GWP42003-P v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9513 ^[5]
Method	Mixed models for repeated measures
Parameter estimate	Least square mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	1.42
Variability estimate	Standard error of the mean
Dispersion value	0.695

Notes:

[5] - Mixed models for repeated measures (MMRM) model includes randomization stratification factors, baseline score, visit, treatment arm, visit by treatment arm interaction as fixed effects, and visit repeated within each patient as a repeated effect.

Statistical analysis title	Hyperactivity/Noncompliance: GWP42003-P vs Placebo
Statistical analysis description:	
Superiority analysis at Week 12	
Comparison groups	GWP42003-P v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.305 ^[6]
Method	Mixed models for repeated measures
Parameter estimate	Least square mean difference
Point estimate	2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.86
upper limit	5.88
Variability estimate	Standard error of the mean
Dispersion value	1.943

Notes:

[6] - Mixed models for repeated measures (MMRM) model includes randomization stratification factors, baseline score, visit, treatment arm, visit by treatment arm interaction as fixed effects, and visit repeated within each patient as a repeated effect.

Statistical analysis title	Inappropriate Speech: GWP42003-P vs Placebo (WK12)
Statistical analysis description:	
Superiority analysis	

Comparison groups	GWP42003-P v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4754 ^[7]
Method	Mixed models for repeated measures
Parameter estimate	Least square mean difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.66
Variability estimate	Standard error of the mean
Dispersion value	0.517

Notes:

[7] - Mixed models for repeated measures (MMRM) model includes randomization stratification factors, baseline score, visit, treatment arm, visit by treatment arm interaction as fixed effects, and visit repeated within each patient as a repeated effect.

Primary: Change from Baseline in Vineland Adaptive Behavior Scales-3 (VABS-3) Scores

End point title	Change from Baseline in Vineland Adaptive Behavior Scales-3 (VABS-3) Scores
-----------------	---

End point description:

The VABS-3 scales assess what a person does, rather than what he or she can do. The Vineland-3 assesses adaptive behavior in 3 domains: Communication, Daily Living Skills, and Socialization. Each domain is comprised of 3 subdomains: receptive expression and written (communication); personal, domestic and community (daily living skills); Interpersonal relationships, play and leisure and copying skills (socialization).

End point type	Primary
----------------	---------

End point timeframe:

Baseline up to Week 12

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49 ^[8]	54 ^[9]		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 4	2.97 (± 6.70)	0.99 (± 9.29)		
Week 8	3.69 (± 10.82)	3.54 (± 8.83)		
Week 12	4.85 (± 8.83)	5.55 (± 10.42)		

Notes:

[8] - WK4: n=37; WK8: n=36; WK12: n=31

[9] - WK4: n=45; WK8: n=40; WK12: n=32

Statistical analyses

Statistical analysis title	GWP42003-P vs Placebo (Week 12)
----------------------------	---------------------------------

Statistical analysis description:

Superiority analysis

Comparison groups	GWP42003-P v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8506 ^[10]
Method	Mixed models for repeated measures
Parameter estimate	Least square mean difference
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.26
upper limit	5.15
Variability estimate	Standard error of the mean
Dispersion value	2.36

Notes:

[10] - Mixed models for repeated measures (MMRM) model includes randomization stratification factors, baseline score, visit, treatment arm, visit by treatment arm interaction as fixed effects, and visit repeated within each patient as a repeated effect.

Primary: Number of Patients Per Clinical Global Impression Improvement (CGI-I) Category

End point title	Number of Patients Per Clinical Global Impression Improvement (CGI-I) Category
-----------------	--

End point description:

The CGI-I is a 7-point scale that requires the clinician to assess how much the patient's illness has improved or worsened relative to a baseline state at the beginning of the intervention. The clinician is asked: Compared to the patient's condition at admission to the project, how much has the patient changed? This is rated as: 1 = very much improved; 2 = much improved; 3 = minimally improved; 4 = no change; 5 = minimally worse; 6 = much worse; or 7 = very much worse. Higher scores indicate worse clinical outcome. The number of patients in each CGI-I category is reported.

End point type	Primary
----------------	---------

End point timeframe:

Day 85

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	38		
Units: number of patients				
number (not applicable)				
Minimally improved	13	14		
Much improved	12	11		
No change	9	11		
Much worse	0	1		
Very much improved	0	1		
Minimally worse	0	0		
Very much worse	0	0		

Statistical analyses

Statistical analysis title	GWP42003-P vs Placebo (Week 12)
Statistical analysis description: Responders with 'Very Much Improved' or 'Much Improved' response at week 12	
Comparison groups	GWP42003-P v Placebo
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7087 ^[11]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	3.51

Notes:

[11] - Logistic regression model includes treatment arm, randomization stratification variables and baseline score (CGI-S) as covariates. Responders are those who achieved a score of 1 or 2 ('Very Much Improved' or 'Much Improved') at post-baseline visits.

Primary: Change from Baseline in Clinical Global Impression Severity (CGI-S) Scores

End point title	Change from Baseline in Clinical Global Impression Severity (CGI-S) Scores
-----------------	--

End point description:

The CGI-S is a 7-point scale that requires the clinician to rate the severity of the patient's illness at the time of assessment, relative to the clinician's experience with patients who have the same diagnosis. The clinician is asked: Considering your total clinical experience with this particular population, how ill is the patient at this time? This is rated as: 1 = normal, not at all ill; 2 = borderline ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; or 7 = extremely ill. Higher scores indicate worse outcome. The change from baseline in CGI-S scores is reported and lower mean scores indicate better outcome.

End point type	Primary
----------------	---------

End point timeframe:

Baseline up to Week 12

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49 ^[12]	54 ^[13]		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 4	-0.33 (± 0.61)	-0.31 (± 0.69)		
Week 8	-0.50 (± 0.68)	-0.48 (± 0.92)		
Week 12	-0.55 (± 0.85)	-0.63 (± 1.10)		

Notes:

[12] - WK4: n=43; WK8: n=40; WK12: n=31

[13] - WK4: n=51; WK8: n=42; WK12: n=32

Statistical analyses

Statistical analysis title	GWP42003-P vs Placebo (Week 12)
Statistical analysis description:	
Superior analysis	
Comparison groups	GWP42003-P v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6108
Method	Cochran-Mantel-Haenszel

Secondary: Number of Patients Reporting Treatment-emergent Adverse Events

End point title	Number of Patients Reporting Treatment-emergent Adverse Events
End point description:	
A TEAE is one that started, or worsened in severity or seriousness, following the first dose of IMP. AEs were coded according to the Medical Dictionary for Regulatory Activities v24.0 dictionary.	
End point type	Secondary
End point timeframe:	
Baseline up to Day 106	

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	54		
Units: number of patients				
number (not applicable)				
TEAE	27	24		
Non-TEAE	25	32		
Treatment-related TEAE	6	10		
Serious TEAE	2	1		
Serious treatment-related TEAE	0	0		
TEAE leading to study intervention withdrawal	2	1		
Treatment-related TEAE leading to drug withdrawal	1	1		
TEAE leading to withdrawal	2	2		
TEAE leading to death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Hematology Clinical Laboratory Levels

End point title	Mean Change from Baseline in Hematology Clinical Laboratory Levels
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline up to Week 9 (end of taper/withdrawal)

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	37		
Units: 10 ⁹ /L				
arithmetic mean (standard deviation)				
Week 9: Basophils	-0.01 (± 0.03)	0 (± 0.03)		
Week 9: Eosinophils	-0.09 (± 0.311)	0 (± 0.40)		
Week 9: Lymphocytes	0.04 (± 0.70)	-0.20 (± 0.68)		
Week 9: Monocytes	-0.01 (± 0.15)	-0.01 (± 0.19)		
Week 9: Neutrophils	0.04 (± 1.80)	-0.01 (± 1.26)		
Week 9: Platelets	-9.43 (± 34.50)	8.43 (± 52.13)		
Week 9: Leukocytes	-0.02 (± 1.87)	-0.23 (± 1.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Hematology Clinical Laboratory Levels

End point title	Mean Percentage Change from Baseline in Hematology Clinical Laboratory Levels
-----------------	---

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline up to Week 9 (end of taper/withdrawal)

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30 ^[14]	37 ^[15]		
Units: percentage change from baseline				
arithmetic mean (standard deviation)				
Week 9: Basophils/Leukocytes	-0.07 (± 0.45)	-0.03 (± 0.42)		
Week 9: Eosinophils/Leukocytes	-1.33 (± 5.37)	0.22 (± 4.88)		
Week 9: Hematocrit	-0.02 (± 2.19)	0.43 (± 2.30)		
Week 9: Lymphocytes/Leukocytes	1.05 (± 11.25)	-2.32 (± 8.26)		

Week 9: Monocytes/Leukocytes	-0.16 (\pm 2.04)	0.05 (\pm 1.86)		
Week 9: Neutrophils/Leukocytes	0.49 (\pm 12.29)	2.08 (\pm 8.89)		

Notes:

[14] - Hematocrit: n=31

[15] - Hematocrit: n=38

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Hemoglobin Levels

End point title	Mean Change from Baseline in Hemoglobin Levels
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Week 9 (end of taper/withdrawal)

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	38		
Units: g/dL				
arithmetic mean (standard deviation)				
Week 9	-0.06 (\pm 0.55)	0.08 (\pm 0.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Erythrocyte Mean Corpuscular Hemoglobin Levels

End point title	Mean Change from Baseline in Erythrocyte Mean Corpuscular Hemoglobin Levels
-----------------	---

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Week 9 (end of taper/withdrawal)

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	38		
Units: pg/cell				
arithmetic mean (standard deviation)				
Week 9	0.13 (± 0.67)	-0.03 (± 0.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Erythrocyte Mean Corpuscular Volume Levels

End point title	Mean Change from Baseline in Erythrocyte Mean Corpuscular Volume Levels
End point description:	
End point type	Secondary
End point timeframe:	
Week 9 (end of taper/withdrawal)	

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	38		
Units: fL				
arithmetic mean (standard deviation)				
Week 9	0.52 (± 2.32)	0.03 (± 2.39)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients with Clinically Significant Vital Sign Values

End point title	Number of Patients with Clinically Significant Vital Sign Values
End point description:	
End point type	Secondary
End point timeframe:	
Post-baseline	

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45 ^[16]	52 ^[17]		
Units: patients				
number (not applicable)				
Increase in weight from baseline >7%	7	13		
Decrease in weight from baseline >7%	2	2		
Body temperature <36 degrees Celsius	4	6		
Body temperature >38 degrees Celsius	1	0		
Pulse rate <60 beats/min	1	3		
Pulse rate >100 beats/min	7	4		
Respiratory rate <12 breaths/min	0	0		
Respiratory rate >20 breaths/min	13	17		
Systolic blood pressure <90 mmhg	5	3		
Systolic blood pressure >160 mmhg	0	0		
Diastolic blood pressure <50 mmhg	3	2		
Diastolic blood pressure >120 mmhg	0	0		

Notes:

[16] - Weight: n=41; Respiratory rate: n=43

[17] - Weight: n=49

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients with Clinically Significant Physical Examination Procedure Findings

End point title	Number of Patients with Clinically Significant Physical Examination Procedure Findings
End point description:	
Number of patients with abnormal physical exam findings are reported.	
End point type	Secondary
End point timeframe:	
Baseline up to Day 85 post-baseline	

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	54		
Units: patients				
number (not applicable)				
Abdomen	2	0		
Cardiovascular	0	0		
Chest/lungs	0	0		
Dermatological	3	3		
Endocrine system	0	0		
Gastrointestinal	0	0		
General appearance	0	2		
HEENT	0	1		
Lymphatic	0	0		

Musculoskeletal/Extremities	0	1		
Neurological	2	0		
Other	0	0		
Genitourinary/Reproductive	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients with Clinically Significant 12-lead Electrocardiogram Findings

End point title	Number of Patients with Clinically Significant 12-lead Electrocardiogram Findings
-----------------	---

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline up to Day 85 post-baseline

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	54		
Units: patients				
number (not applicable)				
QTcB >450 msec	7	4		
QTcB >480 msec	2	0		
QTcB >500 msec	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Reporting Suicidal Ideation or Behavior Using the Columbia-Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Patients Reporting Suicidal Ideation or Behavior Using the Columbia-Suicide Severity Rating Scale (C-SSRS)
-----------------	--

End point description:

C-SSRS rating scale results since last visit is reported.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline up to Day 92

End point values	GWP42003-P	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	54		
Units: patients				
number (not applicable)				
Suicidal ideation	4	3		
Wish to be dead	3	3		
Non-specific active suicidal thoughts	2	1		
Active suicidal ideation, no intent to act	1	0		
Active suicidal ideation, some intent to act	0	0		
Active suicidal ideation, specific plan/intent	0	0		
Suicidal behavior	3	6		
Actual attempt	0	1		
Interrupted attempt	0	1		
Aborted attempt	0	0		
Preparatory acts or behavior	0	1		
Suicidal behavior item	0	1		
Self-injurious behavior without suicidal intent	3	5		
Completed suicide	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from baseline up to 14 days after last dose, up to approximately 12 weeks.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24
--------------------	----

Reporting groups

Reporting group title	GWP42003-P
-----------------------	------------

Reporting group description:

Patients who were randomized to 5 mg/kg/day GWP42003-P for 1 week and then 10 mg/kg/day GWP42003-P. At the end of treatment, participants tapered off the medication over a period of 1 week.

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Patients who were randomized to placebo for 12 weeks.

Serious adverse events	GWP42003-P	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 49 (4.08%)	1 / 54 (1.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 49 (2.04%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 49 (2.04%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GWP42003-P	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 49 (28.57%)	20 / 54 (37.04%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 49 (6.12%)	4 / 54 (7.41%)	
occurrences (all)	3	4	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 49 (0.00%)	5 / 54 (9.26%)	
occurrences (all)	0	5	
Fatigue			
subjects affected / exposed	0 / 49 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	7 / 49 (14.29%)	4 / 54 (7.41%)	
occurrences (all)	7	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 49 (6.12%)	0 / 54 (0.00%)	
occurrences (all)	3	0	
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 49 (0.00%)	5 / 54 (9.26%)	
occurrences (all)	0	5	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 49 (8.16%)	0 / 54 (0.00%)	
occurrences (all)	4	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 49 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	

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

None reported