



Clinical trial results:

A Randomized, Double-blind, Placebo-controlled Trial to Investigate the Efficacy and Safety of Cannabidiol (CBD; GWP42003-P) in Infants with Infantile Spasms Following an Initial Open-label Pilot Study

Summary

EudraCT number	2015-004904-50
Trial protocol	PL
Global end of trial date	13 June 2019

Results information

Result version number	v1
This version publication date	29 December 2019
First version publication date	29 December 2019

Trial information

Trial identification

Sponsor protocol code	GWEP15100
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	Medical Enquiries, GW Research Ltd, medinfo@gwpharm.com
Scientific contact	Medical Enquiries, GW Research Ltd, medinfo@gwpharm.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001964-PIP01-16
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 June 2019
Global end of trial reached?	Yes
Global end of trial date	13 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the efficacy and safety of CBD (GWP42003-P) in subjects with infantile spasms (IS) who have failed to become spasm free following treatment with 1 or more approved IS therapies.

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles that have their origin in the World Medical Association (WMA) Declaration of Helsinki, adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and subsequent amendments. This trial was also designed to comply with ICH E6 Guideline for good clinical practice (EMA/CHMP/ICH/135/1995) and the European Clinical Trial Directive 2001/20/EC. The International Council for Harmonisation adopted guidelines and other relevant international guidelines, recommendations and requirements were taken into account as comprehensively as possible, as long as they did not violate Polish or US law.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Poland: 1
Worldwide total number of subjects	9
EEA total number of subjects	1

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)	9
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were screened to assess their eligibility to enter the trial within 7 days prior to the first dose administration.

Period 1

Period 1 title	Pilot
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Pilot, Cohort 1: GWP42003-P

Arm description:

Subjects 6 month to 24 months of age received GWP42003-P for 14 days. Starting Day 1 and over the course of 4 days, subjects titrated up to a tolerable dose, not to exceed the target dose of 40 milligrams per kilogram per day (mg/kg/day) of GWP42003-P.

Arm type	Experimental
Investigational medicinal product name	GWP42003-P
Investigational medicinal product code	GWP42003-P
Other name	EPIDIOLEX, cannabidiol, CBD-OS
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered GWP42003-P twice daily or three times daily if poorly tolerated. The dosage was split evenly across the two or three daily administrations to equal a total dose of 40mg/kg/day. Oral liquid formulation that is clear and colorless to yellow in appearance (100 mg/mL), in sesame oil with anhydrous ethanol added sweetener (sucralose) and strawberry flavoring. The oral liquid formulation was administered with a syringe.

Arm title	Pilot, Cohort 2: GWP42003-P
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Arm description:

Subjects 1 month to 24 months of age received GWP42003-P for 14 days. Starting Day 1 and over the course of 4 days, subjects titrated up to a tolerable dose, not to exceed the target dose of 40 milligrams per kilogram per day (mg/kg/day) of GWP42003-P.

Arm type	Experimental
Investigational medicinal product name	GWP42003-P
Investigational medicinal product code	GWP42003-P
Other name	EPIDIOLEX, cannabidiol, CBD-OS
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered GWP42003-P, orally, twice daily or three times daily if poorly tolerated. The dosage was split evenly across the two or three daily administrations to equal the target or most tolerable dose. Oral liquid formulation that is clear and colorless to yellow in appearance (100 mg/mL), in sesame oil with anhydrous ethanol added sweetener (sucralose) and strawberry flavoring. The oral liquid formulation was administered with a syringe.

Number of subjects in period 1	Pilot, Cohort 1: GWP42003-P	Pilot, Cohort 2: GWP42003-P
Started	5	4
Completed	5	4

Period 2

Period 2 title	Open Label Extension (OLE)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	OLE: GWP42003-P
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Arm description:

Following completion of the pilot period, subjects were eligible to participate in the OLE period. Subjects continued their same dose administered in the pilot period for a maximum of 1 year and completed a 10 day taper after completing the study or withdrawing.

Arm type	Experimental
Investigational medicinal product name	GWP42003-P
Investigational medicinal product code	GWP42003-P
Other name	EPIDIOLEX, cannabidiol, CBD-OS
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered GWP42003-P, orally, twice daily or three times daily if poorly tolerated. The dosage was split evenly across the two or three daily administrations to equal the target or most tolerable dose. Oral liquid formulation that is clear and colorless to yellow in appearance (100 mg/mL), in sesame oil with anhydrous ethanol added sweetener (sucralose) and strawberry flavoring. The oral liquid formulation was administered with a syringe.

Number of subjects in period 2	OLE: GWP42003-P
Started	9
Completed	2
Not completed	7
Not specified	1
Subject not receiving any benefit	3
Withdrawn consent by subject or caregiver	3

Baseline characteristics

Reporting groups

Reporting group title	Pilot
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Reporting group description: -

Reporting group values	Pilot	Total	
Number of subjects	9	9	
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	9	9	
Age continuous			
Units: months			
arithmetic mean	12.2		
standard deviation	± 5.56	-	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	3	3	
Race			
Units: Subjects			
White	8	8	
Other, not specified	1	1	

End points

End points reporting groups

Reporting group title	Pilot, Cohort 1: GWP42003-P
Reporting group description: Subjects 6 month to 24 months of age received GWP42003-P for 14 days. Starting Day 1 and over the course of 4 days, subjects titrated up to a tolerable dose, not to exceed the target dose of 40 milligrams per kilogram per day (mg/kg/day) of GWP42003-P.	
Reporting group title	Pilot, Cohort 2: GWP42003-P
Reporting group description: Subjects 1 month to 24 months of age received GWP42003-P for 14 days. Starting Day 1 and over the course of 4 days, subjects titrated up to a tolerable dose, not to exceed the target dose of 40 milligrams per kilogram per day (mg/kg/day) of GWP42003-P.	
Reporting group title	OLE: GWP42003-P
Reporting group description: Following completion of the pilot period, subjects were eligible to participate in the OLE period. Subjects continued their same dose administered in the pilot period for a maximum of 1 year and completed a 10 day taper after completing the study or withdrawing.	
Subject analysis set title	Pilot, All Subjects
Subject analysis set type	Full analysis
Subject analysis set description: This analysis set includes all subjects from both Cohort 1 and Cohort 2 in the Pilot Period.	

Primary: Pilot and OLE: Number of subjects with clinically significant electrocardiogram findings

End point title	Pilot and OLE: Number of subjects with clinically significant electrocardiogram findings ^[1]
End point description: Clinical significance was determined by the investigator. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.	
End point type	Primary
End point timeframe: Pilot, up to Day 15 OLE, up to Day 389	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No stat analysis conducted for this outcome measure.	

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[2]	9 ^[3]		
Units: subjects	0	0		

Notes:

[2] - Safety Analysis Set

[3] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Pilot and OLE: Number of subjects with clinically significant physical examination findings

End point title	Pilot and OLE: Number of subjects with clinically significant physical examination findings ^[4]
End point description: Clinical significance was determined by the investigator. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.	
End point type	Primary
End point timeframe: Pilot, up to Day 15 OLE, up to Day 389	

Notes:

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

Justification: No stat analysis conducted for this outcome measure.

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	g ^[5]	g ^[6]		
Units: subjects	0	0		

Notes:

[5] - Safety Analysis Set

[6] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Pilot and OLE: Number of subjects with clinically significant vital sign findings

End point title	Pilot and OLE: Number of subjects with clinically significant vital sign findings ^[7]
End point description: Clinical significance was determined by the investigator. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.	
End point type	Primary
End point timeframe: Pilot, up to Day 15 OLE, up to Day 389	

Notes:

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

Justification: No stat analysis conducted for this outcome measure.

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	g ^[8]	g ^[9]		
Units: subjects	0	0		

Notes:

[8] - Safety Analysis Set

[9] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Pilot and OLE: Number of subjects with severe treatment-emergent adverse events (TEAEs)

End point title	Pilot and OLE: Number of subjects with severe treatment-emergent adverse events (TEAEs) ^[10]
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End point description:

TEAEs are defined as AEs not present prior to the first investigational medicinal product (IMP) or placebo administration or any event already present that worsened in severity or frequency following IMP exposure. A TEAE occurred if the event was continuous from Baseline and was serious; IMP related; or resulted in death, discontinuation, interruption, or reduction of IMP. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

End point type	Primary
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End point timeframe:

Pilot, up to Day 15

OLE, up to Day 417

Notes:

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

Justification: No stat analysis conducted for this outcome measure.

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[11]	9 ^[12]		
Units: subjects	7	6		

Notes:

[11] - Safety Analysis Set

[12] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Pilot: Number of responders

End point title	Pilot: Number of responders ^[13]
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End point description:

A responder is defined as a subject experiencing a resolution of hypersarrhythmia and free of spasms. Testing for responders was conducted by video-electroencephalography (EEG) for at least 8 hours and up to 24 hours. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

End point type	Primary
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End point timeframe:

Pilot, Baseline to Day 15

Notes:

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

Justification: No stat analysis conducted for this outcome measure.

End point values	Pilot, Cohort 1: GWP42003-P	Pilot, Cohort 2: GWP42003-P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5 ^[14]	4 ^[15]		
Units: subjects	0	0		

Notes:

[14] - Safety Analysis Set

[15] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Pilot: Percentage of responders

End point title	Pilot: Percentage of responders ^[16]
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End point description:

A responder is defined as a subject experiencing a resolution of hypsarrhythmia and free of spasms. Testing for responders was conducted by video-electroencephalography (EEG) for at least 8 hours and up to 24 hours. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

End point type	Primary
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End point timeframe:

Pilot, Baseline to Day 15

Notes:

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

Justification: No stat analysis conducted for this outcome measure.

End point values	Pilot, Cohort 1: GWP42003-P	Pilot, Cohort 2: GWP42003-P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5 ^[17]	4 ^[18]		
Units: percentage				
number (not applicable)	0	0		

Notes:

[17] - Safety Analysis Set

[18] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Pilot and OLE: Number of subjects with any low or high hematology laboratory parameter value

End point title	Pilot and OLE: Number of subjects with any low or high hematology laboratory parameter value ^[19]
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End point description:

Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999=No analysis was conducted for this treatment arm at this time point.

n=number of subjects with evaluable data.

End point type	Primary
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End point timeframe:

Pilot, Day 1 to OLE, End of Taper, Day 389

Notes:

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

Justification: No stat analysis conducted for this outcome measure.

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[20]	9 ^[21]		
Units: subjects				
Pilot, Day 4, Low, n=9	999	4		
Pilot, Day 4, High, n=9	999	4		
Pilot, Day 15, Low, n=8	999	1		
Pilot, Day 15, High, n=8	999	3		
OLE, Day 19, Low, n=8	3	999		
OLE, Day 19, High, n=8	4	999		
OLE, Day 29, Low, n=8	3	999		
OLE, Day 29, High, n=8	4	999		
OLE, Day 43, Low, n=6	1	999		
OLE, Day 43, High, n=6	2	999		
OLE, Day 71, Low, n=5	1	999		
OLE, Day 71, High, n=5	3	999		
OLE, Day 127, Low, n=5	1	999		
OLE, Day 127, High, n=5	3	999		
OLE, Day 211, Low, n=3	1	999		
OLE, Day 211, High, n=3	2	999		
OLE, Day 295, Low, n=3	2	999		
OLE, Day 295, High, n=3	0	999		
OLE, Day 379, Low, n=7	4	999		
OLE, Day 379, High, n=7	4	999		
OLE, Day 389, Low, n=6	1	999		
OLE, Day 389, High, n=6	4	999		

Notes:

[20] - Safety Analysis Set

[21] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Pilot and OLE: Number of subjects with any low or high biochemistry laboratory parameter value

End point title	Pilot and OLE: Number of subjects with any low or high biochemistry laboratory parameter value ^[22]
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End point description:

Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999=No analysis was conducted for this treatment arm at this time point.

n=number of subjects with evaluable data.

End point type	Primary
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End point timeframe:

Pilot, Day 1 to OLE, End of Taper, Day 389

Notes:

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

Justification: No stat analysis conducted for this outcome measure.

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[23]	9 ^[24]		
Units: subjects				
Pilot, Day 4, Low, n=9	999	7		
Pilot, Day 4, High, n=9	999	5		
Pilot, Day 15, Low, n=8	999	5		
Pilot, Day 15, High, n=8	999	5		
OLE, Day 19, Low, n=9	6	999		
OLE, Day 19, High, n=9	7	999		
OLE, Day 29, Low, n=8	6	999		
OLE, Day 29, High, n=8	6	999		
OLE, Day 43, Low, n=6	4	999		
OLE, Day 43, High, n=6	5	999		
OLE, Day 71, Low, n=5	2	999		
OLE, Day 71, High, n=5	4	999		
OLE, Day 127, Low, n=5	4	999		
OLE, Day 127, High, n=5	3	999		
OLE, Day 211, Low, n=3	2	999		
OLE, Day 211, High, n=3	3	999		
OLE, Day 295, Low, n=3	2	999		
OLE, Day 295, High, n=3	3	999		
OLE, Day 379, Low, n=7	5	999		
OLE, Day 379, High, n=7	7	999		
OLE, Day 389, Low, n=5	3	999		
OLE, Day 389, High, n=5	2	999		

Notes:

[23] - Safety Analysis Set

[24] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Pilot and OLE: Number of subjects with any clinically relevant urinalysis parameter value

End point title	Pilot and OLE: Number of subjects with any clinically relevant urinalysis parameter value ^[25]
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End point description:

Clinical significance was determined by the investigator. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999=No analysis was conducted for this treatment arm at this time point.

n=number of subjects with evaluable data.

End point type	Primary
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End point timeframe:

Pilot, Day 1 to OLE, End of Taper, Day 389

Notes:

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

Justification: No stat analysis conducted for this outcome measure.

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[26]	9 ^[27]		
Units: subjects				
Pilot, Day 4, n=7	999	0		
Pilot, Day 15, n=9	999	0		
OLE, Day 19, n=7	0	999		
OLE, Day 29, n=7	0	999		
OLE, Day 43, n=6	0	999		
OLE, Day 71, n=5	1	999		
OLE, Day 127, n=4	0	999		
OLE, Day 211, n=3	0	999		
OLE, Day 295, n=2	0	999		
OLE, Day 379, n=6	0	999		
OLE, Day 389, n=3	0	999		

Notes:

[26] - Safety Analysis Set

[27] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Pilot and OLE: Number of subjects free of clinical spasms

End point title	Pilot and OLE: Number of subjects free of clinical spasms
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End point description:

Clinical spasms were determined by video-EEG for at least 8 hours and up to 24 hours. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999=No analysis was conducted for this treatment arm at this time point.

n=number of subjects with evaluable data.

End point type	Secondary
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End point timeframe:

Pilot, Day 1 to OLE, Day 379

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[28]	9 ^[29]		
Units: subjects				
Pilot, Day 15, n=0,9	999	0		
OLE, Day 29, n=8,0	1	999		
OLE, Day 43, n=6,0	2	999		
OLE, Day 127, n=4,0	1	999		
OLE, Day 211, n=3,0	1	999		
OLE, Day 295, n=2,0	1	999		
OLE, Day 379, n=7,0	3	999		

Notes:

[28] - Safety Analysis Set

[29] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Pilot and OLE: Percentage of subjects free of clinical spasms

End point title	Pilot and OLE: Percentage of subjects free of clinical spasms
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End point description:

Clinical spasms were determined by video-EEG for at least 8 hours and up to 24 hours. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999=No analysis was conducted for this treatment arm at this time point.

n=number of subjects with evaluable data.

End point type	Secondary
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End point timeframe:

Pilot, Day 1 to OLE, Day 379

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[30]	9 ^[31]		
Units: percent				
number (not applicable)				
Pilot, Day 15, n=0, 9	999	0		
OLE, Day 29, n=8,0	11.1	999		
OLE, Day 43, n=6,0	22.2	999		
OLE, Day 127, n=4,0	11.1	999		
OLE, Day 211, n=3,0	11.1	999		
OLE, Day 295, n=2,0	11.1	999		
OLE, Day 379, n=7,0	33.3	999		

Notes:

[30] - Safety Analysis Set

[31] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Pilot and OLE: Number of subjects with a resolution of hypsarrhythmia

End point title	Pilot and OLE: Number of subjects with a resolution of hypsarrhythmia
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End point description:

Resolution of hypsarrhythmia was determined by video-EEG for at least 8 hours and up to 24 hours. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999=No analysis was conducted for this treatment arm at this time point.
n=number of subjects with evaluable data.

End point type	Secondary
End point timeframe:	
Pilot: Day 1 to OLE, Day 379	

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[32]	9 ^[33]		
Units: subjects				
Pilot, Day 15, n=0, 9	999	0		
OLE, Day 29, n=8,0	1	999		
OLE, Day 43, n=6,0	0	999		
OLE, Day 127, n=4,0	1	999		
OLE, Day 211, n=3,0	0	999		
OLE, Day 295, n=2,0	1	999		
OLE, Day 379, n=7,0	3	999		

Notes:

[32] - Safety Analysis Set

[33] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Pilot and OLE: Percentage of subjects with a resolution of hypsarrhythmia

End point title	Pilot and OLE: Percentage of subjects with a resolution of hypsarrhythmia
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End point description:

Resolution of hypsarrhythmia was determined by video-EEG for at least 8 hours and up to 24 hours. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999=No analysis was conducted for this treatment arm at this time point.

n=number of subjects with evaluable data.

End point type	Secondary
End point timeframe:	
Pilot, Day 1 to OLE, Day 379	

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[34]	9 ^[35]		
Units: percent				
number (not applicable)				
Pilot, Day 15, n=0,9	999	0		
OLE, Day 29, n=8,0	11.1	999		
OLE, Day 43, n=6,0	0	999		

OLE, Day 127, n=4,0	11.1	999		
OLE, Day 211, n=3,0	0	999		
OLE, Day 295, n=2,0	11.1	999		
OLE, Day 379, n=7,0	33.3	999		

Notes:

[34] - Safety Analysis Set

[35] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Pilot and OLE: Number of subjects experiencing spasms and seizures subtypes

End point title	Pilot and OLE: Number of subjects experiencing spasms and seizures subtypes
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End point description:

Caregivers recorded subject's spasms and seizures by category in a daily diary. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P. 999=No analysis was conducted for this treatment arm at this time point.

End point type	Secondary
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End point timeframe:

Pilot, Day 1 to OLE, Day 379

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[36]	9 ^[37]		
Units: subjects				
Pilot, Day 4, Clonic	999	0		
Pilot, Day 4, Tonic-Clonic	999	1		
Pilot, Day 4, Atonic	999	0		
Pilot, Day 4, Myoclonic	999	0		
Pilot, Day 4, Focal	999	1		
Pilot, Day 4, Absence	999	0		
Pilot, Day 4, Not Done	999	0		
Pilot, Day 15, Clonic	999	0		
Pilot, Day 15, Tonic-Clonic	999	0		
Pilot, Day 15, Atonic	999	0		
Pilot, Day 15, Myoclonic	999	0		
Pilot, Day 15, Focal	999	2		
Pilot, Day 15, Absence	999	0		
Pilot, Day 15, Not Done	999	0		
OLE, Day 19, Clonic	0	999		
OLE, Day 19, Tonic-Clonic	0	999		
OLE, Day 19, Atonic	0	999		
OLE, Day 19, Myoclonic	0	999		
OLE, Day 19, Focal	1	999		
OLE, Day 19, Absence	0	999		
OLE, Day 19, Not Done	0	999		

OLE, Day 29, Clonic	0	999		
OLE, Day 29, Tonic-Clonic	0	999		
OLE, Day 29, Atonic	0	999		
OLE, Day 29, Myoclonic	0	999		
OLE, Day 29, Focal	1	999		
OLE, Day 29, Absence	0	999		
OLE, Day 29, Not Done	0	999		
OLE, Day 127, Clonic	0	999		
OLE, Day 127, Tonic-Clonic	1	999		
OLE, Day 127, Atonic	0	999		
OLE, Day 127, Myoclonic	1	999		
OLE, Day 127, Focal	0	999		
OLE, Day 127, Absence	1	999		
OLE, Day 127, Not Done	0	999		
OLE, Day 211, Clonic	0	999		
OLE, Day 211, Tonic-Clonic	1	999		
OLE, Day 211, Atonic	0	999		
OLE, Day 211, Myoclonic	0	999		
OLE, Day 211, Focal	0	999		
OLE, Day 211, Absence	1	999		
OLE, Day 211, Not Done	0	999		
OLE, Day 295, Clonic	0	999		
OLE, Day 295, Tonic-Clonic	1	999		
OLE, Day 295, Atonic	1	999		
OLE, Day 295, Myoclonic	0	999		
OLE, Day 295, Focal	0	999		
OLE, Day 295, Absence	1	999		
OLE, Day 295, Not Done	0	999		
OLE, Day 379, Clonic	1	999		
OLE, Day 379, Tonic-Clonic	1	999		
OLE, Day 379, Atonic	0	999		
OLE, Day 379, Myoclonic	0	999		
OLE, Day 379, Focal	1	999		
OLE, Day 379, Absence	1	999		
OLE, Day 379, Not Done	0	999		

Notes:

[36] - Safety Analysis Set

[37] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Pilot and OLE: Average time to cessation of spasms

End point title	Pilot and OLE: Average time to cessation of spasms
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End point description:

Analysis could not be conducted for this end point. This study met No Go Criteria, in that all 9 patients enrolled in the pilot phase demonstrated continued hypsarrhythmia and spasms on follow-up video EEG after 2 weeks of treatment. The pilot period was terminated and the pivotal period was not initiated; however, all subjects completing the pilot period were eligible to roll into the OLE for a maximum of 1 year.

998=analysis could not be conducted

End point type	Secondary
End point timeframe:	
Pilot, Day 1 to OLE, Day 379	

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9	9		
Units: hours				
arithmetic mean (standard deviation)	998 (± 998)	998 (± 998)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pilot and OLE: Caregiver Global Impression of Change (CGIC)

End point title	Pilot and OLE: Caregiver Global Impression of Change (CGIC)
End point description:	
<p>The CGIC is a single question assessment completed by the caregiver. The question assesses the status of the subject's condition since they've started treatment. The caregiver provides a rating on a 7 point scale from 1-"very much improved" to 7-"very much worse". Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.</p> <p>999=No analysis was conducted for this treatment arm at this time point.</p>	
End point type	Secondary
End point timeframe:	
Pilot, Day 1 to OLE, Day 379	

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[38]	9 ^[39]		
Units: score on a scale				
number (not applicable)				
Pilot, Day 15, Very Much Improved	999	1		
Pilot, Day 15, Much Improved	999	0		
Pilot, Day 15, Slightly Improved	999	7		
Pilot, Day 15, No Change	999	1		
Pilot, Day 15, Slightly Worse	999	0		
Pilot, Day 15, Much Worse	999	0		
Pilot, Day 15, Very Much Worse	999	0		
Pilot, Day 15, Not Done	999	0		
OLE, Day 29, Very Much Improved	1	999		
OLE, Day 29, Much Improved	1	999		
OLE, Day 29, Slightly Improved	5	999		
OLE, Day 29, No Change	1	999		

OLE, Day 29, Slightly Worse	0	999		
OLE, Day 29, Much Worse	0	999		
OLE, Day 29, Very Much Worse	0	999		
OLE, Day 29, Not Done	0	999		
OLE, Day 43, Very Much Improved	2	999		
OLE, Day 43, Much Improved	1	999		
OLE, Day 43, Slightly Improved	3	999		
OLE, Day 43, No Change	0	999		
OLE, Day 43, Slightly Worse	0	999		
OLE, Day 43, Much Worse	0	999		
OLE, Day 43, Very Much Worse	0	999		
OLE, Day 43, Not Done	0	999		
OLE, Day 71, Very Much Improved	3	999		
OLE, Day 71, Much Improved	0	999		
OLE, Day 71, Slightly Improved	1	999		
OLE, Day 71, No Change	0	999		
OLE, Day 71, Slightly Worse	1	999		
OLE, Day 71, Much Worse	0	999		
OLE, Day 71, Very Much Worse	0	999		
OLE, Day 71, Not Done	0	999		
OLE, Day 127, Very Much Improved	2	999		
OLE, Day 127, Much Improved	2	999		
OLE, Day 127, Slightly Improved	0	999		
OLE, Day 127, No Change	0	999		
OLE, Day 127, Slightly Worse	0	999		
OLE, Day 127, Much Worse	0	999		
OLE, Day 127, Very Much Worse	0	999		
OLE, Day 127, Not Done	0	999		
OLE, Day 211, Very Much Improved	1	999		
OLE, Day 211, Much Improved	2	999		
OLE, Day 211, Slightly Improved	0	999		
OLE, Day 211, No Change	0	999		
OLE, Day 211, Slightly Worse	0	999		
OLE, Day 211, Much Worse	0	999		
OLE, Day 211, Very Much Worse	0	999		
OLE, Day 211, Not Done	0	999		
OLE, Day 295, Very Much Improved	1	999		
OLE, Day 295, Much Improved	2	999		
OLE, Day 295, Slightly Improved	0	999		
OLE, Day 295, No Change	0	999		
OLE, Day 295, Slightly Worse	0	999		
OLE, Day 295, Much Worse	0	999		
OLE, Day 295, Very Much Worse	0	999		
OLE, Day 295, Not Done	0	999		
OLE, Day 379, Very Much Improved	2	999		
OLE, Day 379, Much Improved	1	999		
OLE, Day 379, Slightly Improved	3	999		
OLE, Day 379, No Change	0	999		
OLE, Day 379, Slightly Worse	1	999		
OLE, Day 379, Much Worse	1	999		
OLE, Day 379, Very Much Worse	0	999		
OLE, Day 379, Not Done	1	999		

Notes:

[38] - Safety Analysis Set

[39] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Pilot and OLE: Physician Global Impression of Change (PGIC)

End point title	Pilot and OLE: Physician Global Impression of Change (PGIC)
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End point description:

The PGIC is a single question assessment completed by the investigator. The question assesses the status of the subject's condition since they've started treatment. The investigator provides a rating on a 7 point scale from 1-"very much improved" to 7-"very much worse". Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P. 999=No analysis was conducted for this treatment arm at this time point.

End point type	Secondary
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End point timeframe:

Pilot, Day 1 to OLE, Day 379

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[40]	9 ^[41]		
Units: score on a scale				
number (not applicable)				
Pilot, Day 15, Very Much Improved	999	0		
Pilot, Day 15, Much Improved	999	1		
Pilot, Day 15, Slightly Improved	999	5		
Pilot, Day 15, No Change	999	3		
Pilot, Day 15, Slightly Worse	999	0		
Pilot, Day 15, Much Worse	999	0		
Pilot, Day 15, Very Much Worse	999	0		
Pilot, Day 15, Not Done	999	0		
OLE, Day 29, Very Much Improved	1	999		
OLE, Day 29, Much Improved	1	999		
OLE, Day 29, Slightly Improved	2	999		
OLE, Day 29, No Change	4	999		
OLE, Day 29, Slightly Worse	0	999		
OLE, Day 29, Much Worse	0	999		
OLE, Day 29, Very Much Worse	0	999		
OLE, Day 29, Not Done	0	999		
OLE, Day 43, Very Much Improved	1	999		
OLE, Day 43, Much Improved	0	999		
OLE, Day 43, Slightly Improved	4	999		
OLE, Day 43, No Change	1	999		
OLE, Day 43, Slightly Worse	0	999		
OLE, Day 43, Much Worse	0	999		

OLE, Day 43, Very Much Worse	0	999		
OLE, Day 43, Not Done	0	999		
OLE, Day 71, Very Much Improved	1	999		
OLE, Day 71, Much Improved	2	999		
OLE, Day 71, Slightly Improved	1	999		
OLE, Day 71, No Change	1	999		
OLE, Day 71, Slightly Worse	0	999		
OLE, Day 71, Much Worse	0	999		
OLE, Day 71, Very Much Worse	0	999		
OLE, Day 71, Not Done	0	999		
OLE, Day 127, Very Much Improved	1	999		
OLE, Day 127, Much Improved	2	999		
OLE, Day 127, Slightly Improved	1	999		
OLE, Day 127, No Change	0	999		
OLE, Day 127, Slightly Worse	0	999		
OLE, Day 127, Much Worse	0	999		
OLE, Day 127, Very Much Worse	0	999		
OLE, Day 127, Not Done	0	999		
OLE, Day 211, Very Much Improved	0	999		
OLE, Day 211, Much Improved	1	999		
OLE, Day 211, Slightly Improved	1	999		
OLE, Day 211, No Change	1	999		
OLE, Day 211, Slightly Worse	0	999		
OLE, Day 211, Much Worse	0	999		
OLE, Day 211, Very Much Worse	0	999		
OLE, Day 211, Not Done	0	999		
OLE, Day 295, Very Much Improved	0	999		
OLE, Day 295, Much Improved	1	999		
OLE, Day 295, Slightly Improved	0	999		
OLE, Day 295, No Change	1	999		
OLE, Day 295, Slightly Worse	0	999		
OLE, Day 295, Much Worse	1	999		
OLE, Day 295, Very Much Worse	0	999		
OLE, Day 295, Not Done	0	999		
OLE, Day 379, Very Much Improved	0	999		
OLE, Day 379, Much Improved	1	999		
OLE, Day 379, Slightly Improved	3	999		
OLE, Day 379, No Change	2	999		
OLE, Day 379, Slightly Worse	1	999		
OLE, Day 379, Much Worse	1	999		
OLE, Day 379, Very Much Worse	0	999		
OLE, Day 379, Not Done	1	999		

Notes:

[40] - Safety Analysis Set

[41] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of responders

End point title	OLE: Number of responders
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End point description:

A responder is defined as a subject experiencing a resolution of hypersarrhythmia and free of spasms. Testing for responders was conducted by video-electroencephalography (EEG) for at least 8 hours and up to 24 hours. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

n=number of subjects with evaluable data.

End point type	Secondary
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End point timeframe:

OLE, Day 16 to Day 379

End point values	OLE: GWP42003-P			
Subject group type	Reporting group			
Number of subjects analysed	9 ^[42]			
Units: subjects				
OLE, Day 29, n=8	1			
OLE, Day 43, n=6	0			
OLE, Day 127, n=4	0			
OLE, Day 211, n=3	0			
OLE, Day 295, n=2	1			
OLE, Day 379, n=7	3			

Notes:

[42] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Percentage of responders

End point title	OLE: Percentage of responders
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End point description:

A responder is defined as a subject experiencing a resolution of hypersarrhythmia and free of spasms. Testing for responders was conducted by video-electroencephalography (EEG) for at least 8 hours and up to 24 hours. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

n=number of subjects with evaluable data.

End point type	Secondary
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End point timeframe:

OLE, Day 16 to Day 379

End point values	OLE: GWP42003-P			
Subject group type	Reporting group			
Number of subjects analysed	9 ^[43]			
Units: percent				
number (not applicable)				
OLE, Day 29, n=8	11.1			
OLE, Day 43, n=6	0			

OLE, Day 127, n=4	0			
OLE, Day 211, n=3	0			
OLE, Day 295, n=2	11.1			
OLE, Day 379, n=7	33.3			

Notes:

[43] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in height

End point title	OLE: Change from Baseline in height
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End point description:

A positive change indicates an increase in the average subject's height. A negative change indicates a decrease in the average subject's height. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999 = No analysis was conducted for this treatment arm at this time point.

CFB = Change from Baseline

End point type	Secondary
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End point timeframe:

Pilot, Baseline, Day 1 to OLE, End of Taper, Day 389

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[44]	9 ^[45]		
Units: centimeters				
arithmetic mean (standard deviation)				
Pilot, Baseline, Day 1, n=9	999 (\pm 999)	75.04 (\pm 9.557)		
OLE, CFB, Day 29, n=8	0.85 (\pm 0.980)	999 (\pm 999)		
OLE, CFB, Day 43, n=6	0.92 (\pm 1.530)	999 (\pm 999)		
OLE, CFB, Day 71, n=5	3.10 (\pm 0.652)	999 (\pm 999)		
OLE, CFB, Day 127, n=4	3.38 (\pm 1.377)	999 (\pm 999)		
OLE, CFB, Day 211, n=3	5.33 (\pm 1.258)	999 (\pm 999)		
OLE, CFB, Day 295, n=3	8.17 (\pm 1.528)	999 (\pm 999)		
OLE, CFB, Day 379, n=8	5.31 (\pm 4.036)	999 (\pm 999)		
OLE, CFB, Day 389, n=6	3.55 (\pm 4.085)	999 (\pm 999)		

Notes:

[44] - Safety Analysis Set

[45] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in body weight

End point title	OLE: Change from Baseline in body weight
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End point description:

A positive change indicates an increase in the average subject's height. A negative change indicates a decrease in the average subject's height. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999 = No analysis was conducted for this treatment arm at this time point.

CFB=Change from Baseline

End point type	Secondary
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End point timeframe:

Pilot, Baseline, Day 1 to OLE, End of Taper, Day 389

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[46]	9 ^[47]		
Units: kilograms				
arithmetic mean (standard deviation)				
Pilot, Baseline, Day 1, n=9	999 (\pm 999)	9.92 (\pm 3.245)		
OLE, CFB, Day 29, n=8	0.39 (\pm 0.309)	999 (\pm 999)		
OLE, CFB, Day 43, n=6	0.75 (\pm 0.809)	999 (\pm 999)		
OLE, CFB, Day 71, n=5	1.10 (\pm 0.430)	999 (\pm 999)		
OLE, CFB, Day 127, n=4	1.25 (\pm 0.420)	999 (\pm 999)		
OLE, CFB, Day 211, n=3	1.17 (\pm 0.503)	999 (\pm 999)		
OLE, CFB, Day 295, n=3	2.10 (\pm 0.889)	999 (\pm 999)		
OLE, CFB, Day 379, n=9	1.19 (\pm 0.862)	999 (\pm 999)		
OLE, CFB, Day 389, n=6	0.98 (\pm 0.637)	999 (\pm 999)		

Notes:

[46] - Safety Analysis Set

[47] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in head circumference

End point title	OLE: Change from Baseline in head circumference
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End point description:

A positive change indicates an increase in the average subject's head circumference. A negative change indicates a decrease in the average subject's head circumference. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

999 = No analysis was conducted for this treatment arm at this time point.

CFB=Change from Baseline

End point type	Secondary
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End point timeframe:

Pilot, Baseline, Day 1 to OLE, End of Taper, Day 389

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[48]	9 ^[49]		
Units: centimeters				
arithmetic mean (standard deviation)				
Pilot, Baseline, Day 1, n=9	999 (± 999)	44.71 (± 2.724)		
OLE, CFB, Day 29, n=8	-0.01 (± 1.229)	999 (± 999)		
OLE, CFB, Day 43, n=5	0.54 (± 0.288)	999 (± 999)		
OLE, CFB, Day 71, n=5	0.70 (± 0.570)	999 (± 999)		
OLE, CFB, Day 127, n=3	1.50 (± 0.500)	999 (± 999)		
OLE, CFB, Day 211, n=2	0.75 (± 0.354)	999 (± 999)		
OLE, CFB, Day 295, n=3	-0.3 (± 2.31)	999 (± 999)		
OLE, CFB, Day 379, n=8	1.14 (± 1.707)	999 (± 999)		
OLE, CFB, Day 389, n=5	0.90 (± 1.782)	999 (± 999)		

Notes:

[48] - Safety Analysis Set

[49] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in Vineland Adaptive Behavior Scales, Second Edition (Vineland-II) score

End point title	OLE: Change from Baseline in Vineland Adaptive Behavior Scales, Second Edition (Vineland-II) score
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End point description:

The Vineland-II scores were assessed by the subject's caregiver. Caregivers were asked to score questions in following categories the subject's communication, daily living, physical activity, problem behaviors, and social skills and relationships. Scoring was slightly different for each section, but generally ranged from "usually" to "never". Higher scores represent greater levels of functioning and lower skills represent lower levels of functioning. Analysis was conducted in members of the Safety Set, defined as all subjects who had received ≥ 1 dose of GWP42003-P.

n=number of subjects with evaluable data.

CFB=Change from Baseline

End point type	Secondary
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End point timeframe:

Pilot, Baseline, Day 1 to OLE, Day 379

End point values	OLE: GWP42003-P	Pilot, All Subjects		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9 ^[50]	9 ^[51]		
Units: score on a scale				
arithmetic mean (standard deviation)				
Pilot, Baseline, Day 1, n=9	999 (± 999)	33.6 (± 37.27)		
OLE, CFB, Day 211, n=3	6.3 (± 3.51)	999 (± 999)		
OLE, CFB, Day 379, n=9	-5.4 (± 23.42)	999 (± 999)		

Notes:

[50] - Safety Analysis Set

[51] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of subjects with relapse of spasms

End point title	OLE: Number of subjects with relapse of spasms
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End point description:

Analysis could not be conducted for this end point. This study met No Go Criteria, in that all 9 patients enrolled in the pilot phase demonstrated continued hypsarrhythmia and spasms on follow-up video EEG after 2 weeks of treatment. The pilot period was terminated and the pivotal period was not initiated; however, all subjects completing the pilot period were eligible to roll into the OLE for a maximum of 1 year.

998=analysis could not be conducted

End point type	Secondary
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End point timeframe:

OLE Period, Day 16 to Day 379

End point values	OLE: GWP42003-P			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: subjects	998			

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Percentage of subjects with relapse of spasms

End point title	OLE: Percentage of subjects with relapse of spasms
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End point description:

Analysis could not be conducted for this end point. This study met No Go Criteria, in that all 9 patients enrolled in the pilot phase demonstrated continued hypsarrhythmia and spasms on follow-up video EEG after 2 weeks of treatment. The pilot period was terminated and the pivotal period was not initiated; however, all subjects completing the pilot period were eligible to roll into the OLE for a maximum of 1 year.

998=analysis could not be conducted

End point type	Secondary
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End point timeframe:

OLE Period, Day 16 to Day 379

End point values	OLE: GWP42003-P			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
number (not applicable)	998			

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Average time to relapse

End point title	OLE: Average time to relapse
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End point description:

Analysis could not be conducted for this end point. This study met No Go Criteria, in that all 9 patients enrolled in the pilot phase demonstrated continued hypsarrhythmia and spasms on follow-up video EEG after 2 weeks of treatment. The pilot period was terminated and the pivotal period was not initiated; however, all subjects completing the pilot period were eligible to roll into the OLE for a maximum of 1 year.

998=analysis could not be conducted

End point type	Secondary
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End point timeframe:

OLE Period, Day 16 to Day 379

End point values	OLE: GWP42003-P			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: day(s)				
arithmetic mean (standard deviation)	998 (± 998)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Pilot, up to Day 15

OLE, up to Day 417

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) were collected in members of the Safety Population, comprised of all subjects who received at least 1 dose of GWP42003-P. TEAEs are defined as all adverse events not present prior to the first IMP or placebo administration or any event already present that worsened in severity or frequency following IMP.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Open Label Extension (OLE)
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Reporting group description: -

Reporting group title	Pilot
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Reporting group description: -

Serious adverse events	Open Label Extension (OLE)	Pilot	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)	1 / 9 (11.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events		0	
Nervous system disorders			
Status epilepticus			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (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			
Enterovirus infection			
subjects affected / exposed	2 / 9 (22.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			

subjects affected / exposed	2 / 9 (22.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Open Label Extension (OLE)	Pilot	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)	5 / 9 (55.56%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Hypotension			

subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
General disorders and administration site conditions Application site erosion subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Drug tolerance subjects affected / exposed occurrences (all)	 0 / 9 (0.00%) 0 2 / 9 (22.22%) 4 1 / 9 (11.11%) 1	 1 / 9 (11.11%) 1 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Upper respiratory tract congestion subjects affected / exposed occurrences (all) Adenoidal hypertrophy subjects affected / exposed occurrences (all)	 0 / 9 (0.00%) 0 3 / 9 (33.33%) 3 1 / 9 (11.11%) 1	 1 / 9 (11.11%) 1 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0	
Psychiatric disorders Irritability subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all)	 2 / 9 (22.22%) 2 1 / 9 (11.11%) 1	 1 / 9 (11.11%) 1 0 / 9 (0.00%) 0	
Investigations Blood triglycerides increased subjects affected / exposed occurrences (all)	 2 / 9 (22.22%) 2	 0 / 9 (0.00%) 0	
Nervous system disorders Somnolence			

subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	1 / 9 (11.11%) 1	
Myoclonic epilepsy subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Petit mal epilepsy subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2	0 / 9 (0.00%) 0	
Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Middle ear effusion subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Eye disorders Pupils unequal subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	2 / 9 (22.22%) 2	
Constipation subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 9 (11.11%) 1	
Vomiting subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 9 (11.11%) 1	
Gingival pain subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Skin and subcutaneous tissue disorders			

Dermatitis diaper subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Skin irritation subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 9 (11.11%) 1	
Musculoskeletal and connective tissue disorders Scoliosis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	2 / 9 (22.22%) 2	
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 3	0 / 9 (0.00%) 0	
Viral infection subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2	0 / 9 (0.00%) 0	
Bronchiolitis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Ear infection subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	

Otitis media			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Decreased appetite			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Feeding intolerance			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Fluid overload			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Hyponatraemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 May 2016	<ul style="list-style-type: none">-Revised clinical phase and overall design;-Addition of a pilot phase to confirm safety;-Clarification of video-EEG evaluation;-Clarification of cannabidiol metabolites;-Duration of Open-label Extension Phase;-Clarification of procedures following the investigator's decision to discontinue GWP42003-P during the open label extension phase;-Revised eligibility criteria;-Clarification of withdrawal criterion;-Revised pharmacokinetic blood sampling times;-Removal of Caregiver Impression of IMP Palatability Questionnaire;-Removal of THC testing.
18 October 2016	<ul style="list-style-type: none">-Extend age range in the pilot phase; second cohort;-Clarification of allowable changes in concomitant medications;-Utilization of central video electroencephalography readings;-Changes to inclusion/exclusion criteria;-Updated withdrawal criteria;-Changes to information recorded in the paper diary;-Updated statistical considerations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This study met No Go Criteria. Pilot Phase (PP) subjects had continued hypersarrhythmia/spasms after 2 weeks of treatment. The PP was terminated; the pivotal period was not initiated. Subjects completing the PP could roll into the OLE for up to 1 year.

Notes: