Clinical trial results:
A double-blind, randomized, placebo-controlled study to investigate the efficacy and safety of cannabidiol (GWP42003-P, CBD) as add-on therapy in patients with tuberous sclerosis complex who experience inadequately-controlled seizures

Summary

EudraCT number	2015-002154-12
Trial protocol	ES GB PL NL
Global end of trial date	11 June 2021

Results information

Result version number	v1 (current)
This version publication date	26 December 2021
First version publication date	26 December 2021

Trial information

Trial identification

Sponsor protocol code	GWEP1521 Open-Label Extension

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02544750
WHO universal trial number (UTN)	-
Other trial identifiers	GWEP1521 - Open Label Extension: NCT02544750, GWEP1521 - Double Blind Phase: NCT02544763

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	GW Research Ltd Switchboard, GW Research Ltd, 0044 1223266800, info@gwpharm.com
Scientific contact	GW Research Ltd Switchboard, GW Research Ltd, 0044 1223266800, info@gwpharm.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-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	26 August 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Double-Blinded Phase (DBP): To evaluate the efficacy of GWP42003-P as add-on therapy in reducing the frequency of seizures when compared with placebo in subjects with Tuberous Sclerosis Complex (TSC).

Open-label Extension (OLE): To evaluate via the adverse events (AE) profile the long term safety and tolerability of GWP42003-P as add-on therapy in children and adults with TSC who experience inadequately-controlled seizures.

Protection of trial subjects:

This study was conducted in accordance with International Council on Harmonisation (ICH) 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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 April 2016
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	Netherlands: 9
Country: Number of subjects enrolled	Poland: 61
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Australia: 24
Country: Number of subjects enrolled	United States: 112
Worldwide total number of subjects	224
EEA total number of subjects	81

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	10
Children (2-11 years)	108
Adolescents (12-17 years)	48
Adults (18-64 years)	58
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 255 subjects were screened; of these 31 were screen failures. A total of 224 subjects were randomized to double-blind treatment. A total of 199 subjects from the DBP were enrolled in the OLE study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	DBP: GWP42003-P 25 mg/kg/Day

Arm description:

Subjects were randomized to receive GWP42003-P 25 milligrams per kilogram per day (mg/kg/day) orally twice daily (morning and evening administration). Subjects completed a 4-week dose-escalation period, titrating up to their assigned dose, before continuing on a stable dose of blinded GWP42003-P for 12 weeks.

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

Dosage and administration details:

GWP42003-P was presented as an oral solution containing 100 mg/milliliter (mL) cannabidiol (CBD) dissolved in the excipients sesame oil and anhydrous ethanol with added sweetener and strawberry flavoring.

Arm title	DBP: GWP42003-P 50 mg/kg/Day

Arm description:

Subjects were randomized to receive GWP42003-P 50 mg/kg/day orally twice daily (morning and evening administration). Subjects completed a 4-week dose escalation period, titrating up to their assigned dose, before continuing on a stable dose of blinded GWP42003-P for 12 weeks.

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

Dosage and administration details:

GWP42003-P was presented an oral solution containing 100 mg/mL cannabidiol dissolved in the excipients sesame oil and anhydrous ethanol with added sweetener and strawberry flavoring.

Arm title	DBP: Placebo

Arm description:

Subjects were randomized to receive placebo matched to GWP42003-P orally twice daily (morning and evening administration) for 16 weeks.

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

Dosage and administration details:

Subjects received placebo solution dissolved in the excipients sesame oil and anhydrous ethanol with added sweetener and strawberry flavoring.

Number of subjects in period 1	DBP: GWP42003-P 25 mg/kg/Day	DBP: GWP42003-P 50 mg/kg/Day	DBP: Placebo
Started	75	73	76
Completed	65	61	75
Not completed	10	12	1
Withdrawn by parent/guardian	1	1	1
Physician decision	-	1	-
Adverse event, non-fatal	8	8	-
Met withdrawal criteria	-	2	-
Difficulties taking IMP	1	-	-

Period 2

Period 2 title	Open Label Phase (OLE)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)

Arm description:

Subjects who completed the DBP entered a 2-week blinded transition prior to the OLE. During the transition, open-label IMP was titrated up to 25 mg/kg/day whilst blinded IMP was simultaneously tapered down to zero to accommodate those subjects who had been randomized to placebo during the double-blind phase of the study. Transition from the DBP to the OLE were as follows: Subjects receiving placebo during the DBP were titrated up to receive 25 mg/kg/day in OLE phase, subjects receiving 25 mg/kg/day of GWP42003-P during the DBP continued to receive 25 mg/kg/day in OLE phase, subjects receiving 50 mg/kg/day of GWP42003-P during the DBP were tapered (10% per day for 5 days) to receive 25 mg/kg/day of GWP42003-P during OLE. All subjects completed the transition and entered the OLE taking 25 mg/kg/day GWP42003-P.

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

Dosage and administration details:

GWP42003-P was presented an oral solution containing 100 mg/milliliter (mL) cannabidiol (CBD) dissolved in the excipients sesame oil and anhydrous ethanol with added sweetener and strawberry flavoring.

Arm title	OLE: Placebo (DBP) then GWP42003-P (OLE)

Arm description:

Subjects who completed the DBP entered a 2-week blinded transition prior to the OLE. During the transition, open-label IMP was titrated up to 25 mg/kg/day whilst blinded IMP was simultaneously tapered down to zero to accommodate those subjects who had been randomized to placebo during the double-blind phase of the study. Transition from the DBP to the OLE were as follows: Subjects receiving placebo during the DBP were titrated up to receive 25 mg/kg/day in OLE phase, subjects receiving 25 mg/kg/day of GWP42003-P during the DBP continued to receive 25 mg/kg/day in OLE phase, subjects receiving 50 mg/kg/day of GWP42003-P during the DBP were tapered (10% per day for 5 days) to receive 25 mg/kg/day of GWP42003-P during OLE. All subjects completed the transition and entered the OLE taking 25 mg/kg/day GWP42003-P.

Arm type	Experimental
Investigational medicinal product name	Placebo then GWP42003-P
Investigational medicinal product code	
Other name	Cannabidiol, CBD
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

DBP: Placebo oral solution. OLE: GWP42003-P was presented an oral solution containing 100 mg/mL CBD dissolved in the excipients sesame oil and anhydrous ethanol with added sweetener and strawberry flavoring.

Number of subjects in period 2[1]	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)
Started	124	75
Completed	22	12
Not completed	102	63
Transition To Commercial Product	1	-
Physician decision	3	1
Consent withdrawn by subject	10	4
Adverse event, non-fatal	8	10
Other	69	39
Met withdrawal criteria	2	2
Withdrawal by Parent/Guardian	8	7
Lost to follow-up	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only 199 subjects were transitioned from the DBP to OLE phase. Two subjects did not enter the transition period of the OLE phase.

Baseline characteristics

Reporting groups	
Reporting group title	DBP: GWP42003-P 25 mg/kg/Day
Reporting group description:	
Subjects were randomized to receive GWP42003-P 25 milligrams per kilogram per day (mg/kg/day) orally twice daily (morning and evening administration). Subjects completed a 4-week dose-escalation period, titrating up to their assigned dose, before continuing on a stable dose of blinded GWP42003-P for 12 weeks.	
Reporting group title	DBP: GWP42003-P 50 mg/kg/Day
Reporting group description:	
Subjects were randomized to receive GWP42003-P 50 mg/kg/day orally twice daily (morning and evening administration). Subjects completed a 4-week dose escalation period, titrating up to their assigned dose, before continuing on a stable dose of blinded GWP42003-P for 12 weeks.	
Reporting group title	DBP: Placebo
Reporting group description:	
Subjects were randomized to receive placebo matched to GWP42003-P orally twice daily (morning and evening administration) for 16 weeks.	

Reporting group values	DBP: GWP42003-P 25 mg/kg/Day	DBP: GWP42003-P 50 mg/kg/Day	DBP: Placebo
Number of subjects	75	73	76
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	14.112	12.779	13.794
standard deviation	± 10.8131	± 8.5532	± 10.6143
Gender categorical			
Units: Subjects			
Female	32	30	31
Male	43	43	45
Number of Tuberous Sclerosis Complex (TSC)-Associated Seizures			
TSC-associated seizures included: focal motor seizures without impairment of consciousness or awareness (Type 1 focal motor); focal seizures with impairment of consciousness or awareness (Type 2 focal); focal seizures evolving to bilateral generalized convulsive seizures (Type 3 focal); and tonic-clonic, tonic, clonic, or atonic seizures that are countable. Intent-to-Treat (ITT) Analysis Set: all subjects who were randomized and dosed with IMP in the trial and had post-Baseline efficacy data. Subject data were analyzed according to the treatment group to which they were randomized.			
Units: Seizures			
median	56.0	61.0	54.05
inter-quartile range (Q1-Q3)	21.24 to 101.0	36.00 to 117.0	26.42 to 102.0
Number of Total Seizures			
Total seizures included all seizure types combined. The Baseline Period included all data prior to Day 1. ITT Analysis Set.			
Units: Seizures			
median	56.0	70.0	56.48
inter-quartile range (Q1-Q3)	22.58 to 101.0	38.0 to 130.0	27.50 to 138.10

Reporting group values	Total		
Number of subjects	224		

Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	93		
Male	131		
Number of Tuberous Sclerosis Complex (TSC)-Associated Seizures			
TSC-associated seizures included: focal motor seizures without impairment of consciousness or awareness (Type 1 focal motor); focal seizures with impairment of consciousness or awareness (Type 2 focal); focal seizures evolving to bilateral generalized convulsive seizures (Type 3 focal); and tonic-clonic, tonic, clonic, or atonic seizures that are countable. Intent-to-Treat (ITT) Analysis Set: all subjects who were randomized and dosed with IMP in the trial and had post-Baseline efficacy data. Subject data were analyzed according to the treatment group to which they were randomized.			
Units: Seizures median inter-quartile range (Q1-Q3)	- -		
Number of Total Seizures			
Total seizures included all seizure types combined. The Baseline Period included all data prior to Day 1. ITT Analysis Set.			
Units: Seizures median inter-quartile range (Q1-Q3)	- -		

End points

End points reporting groups

Reporting group title	DBP: GWP42003-P 25 mg/kg/Day

Reporting group description:

Subjects were randomized to receive GWP42003-P 25 milligrams per kilogram per day (mg/kg/day) orally twice daily (morning and evening administration). Subjects completed a 4-week dose-escalation period, titrating up to their assigned dose, before continuing on a stable dose of blinded GWP42003-P for 12 weeks.

Reporting group title	DBP: GWP42003-P 50 mg/kg/Day

Reporting group description:

Subjects were randomized to receive GWP42003-P 50 mg/kg/day orally twice daily (morning and evening administration). Subjects completed a 4-week dose escalation period, titrating up to their assigned dose, before continuing on a stable dose of blinded GWP42003-P for 12 weeks.

Reporting group title	DBP: Placebo

Reporting group description:

Subjects were randomized to receive placebo matched to GWP42003-P orally twice daily (morning and evening administration) for 16 weeks.

Reporting group title	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)

Reporting group description:

Subjects who completed the DBP entered a 2-week blinded transition prior to the OLE. During the transition, open-label IMP was titrated up to 25 mg/kg/day whilst blinded IMP was simultaneously tapered down to zero to accommodate those subjects who had been randomized to placebo during the double-blind phase of the study. Transition from the DBP to the OLE were as follows: Subjects receiving placebo during the DBP were titrated up to receive 25 mg/kg/day in OLE phase, subjects receiving 25 mg/kg/day of GWP42003-P during the DBP continued to receive 25 mg/kg/day in OLE phase, subjects receiving 50 mg/kg/day of GWP42003-P during the DBP were tapered (10% per day for 5 days) to receive 25 mg/kg/day of GWP42003-P during OLE. All subjects completed the transition and entered the OLE taking 25 mg/kg/day GWP42003-P.

Reporting group title	OLE: Placebo (DBP) then GWP42003-P (OLE)

Reporting group description:

Subjects who completed the DBP entered a 2-week blinded transition prior to the OLE. During the transition, open-label IMP was titrated up to 25 mg/kg/day whilst blinded IMP was simultaneously tapered down to zero to accommodate those subjects who had been randomized to placebo during the double-blind phase of the study. Transition from the DBP to the OLE were as follows: Subjects receiving placebo during the DBP were titrated up to receive 25 mg/kg/day in OLE phase, subjects receiving 25 mg/kg/day of GWP42003-P during the DBP continued to receive 25 mg/kg/day in OLE phase, subjects receiving 50 mg/kg/day of GWP42003-P during the DBP were tapered (10% per day for 5 days) to receive 25 mg/kg/day of GWP42003-P during OLE. All subjects completed the transition and entered the OLE taking 25 mg/kg/day GWP42003-P.

Primary: DBP: Percent Change From Baseline in the Number of Tuberous Sclerosis Complex (TSC)-Associated Seizures During the DBP Treatment Period (Maintenance and Titration)

End point title	DBP: Percent Change From Baseline in the Number of Tuberous Sclerosis Complex (TSC)-Associated Seizures During the DBP Treatment Period (Maintenance and Titration)

End point description:

TSC-associated seizures included: focal motor seizures without impairment of consciousness or awareness (Type 1 focal motor); focal seizures with impairment of consciousness or awareness (Type 2 focal); focal seizures evolving to bilateral generalized convulsive seizures (Type 3 focal); and tonic-clonic, tonic, clonic, or atonic seizures that are countable. Percent change from Baseline was calculated as the (post-Baseline value minus the Baseline value) divided by the Baseline value x 100. Intent-to-Treat (ITT) Analysis Set: all subjects who were randomized and dosed with investigational medicinal product (IMP) in the trial and had post-Baseline efficacy data. Data were analyzed according to the treatment group to which subjects were randomized.

End point type	Primary

End point timeframe:
DBP: Baseline; up to Week 16

End point values	DBP: GWP42003-P 25 mg/kg/Day	DBP: GWP42003-P 50 mg/kg/Day	DBP: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	73	76	
Units: Percent change				
median (inter-quartile range (Q1-Q3))	-43.36 (-67.8 to -13.6)	-36.55 (-67.0 to -5.5)	-20.08 (-47.1 to 3.1)	

Statistical analyses

Statistical analysis title	GWP42003-P 25 mg/kg/Day vs Placebo
Comparison groups	DBP: GWP42003-P 25 mg/kg/Day v DBP: Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0009
Method	Mixed model analysis
Parameter estimate	Treatment ratio
Point estimate	0.699
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.567
upper limit	0.861

Statistical analysis title	GWP42003-P 50 mg/kg/Day vs Placebo
Comparison groups	DBP: GWP42003-P 50 mg/kg/Day v DBP: Placebo
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0018
Method	Mixed model analysis
Parameter estimate	Treatment ratio
Point estimate	0.715
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.881

Primary: OLE: Number of Subjects With Any Treatment-emergent Adverse Events (TEAE)

End point title	OLE: Number of Subjects With Any Treatment-emergent Adverse Events (TEAE)[1]

End point description:

An AE was defined as any new unfavorable/unintended signs/symptoms (including abnormal laboratory findings), or diagnosis or worsening of a pre-existing condition, which occurred following screening and at any point up to the post-treatment safety follow-up visit, which may or may not be related to the IMP. Analysis was performed in OLE Safety Analysis Set population defined as all subjects who received at least 1 dose of IMP in the OLE phase of the study.

End point type	Primary

End point timeframe:

OLE: up to approximately 4 years

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: Only descriptive statistics was planned for this endpoint.

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects	117	75		

Statistical analyses

No statistical analyses for this end point

Primary: OLE: Number of Subjects With Related TEAEs, Serious AEs, Discontinuations and Deaths

End point title	OLE: Number of Subjects With Related TEAEs, Serious AEs, Discontinuations and Deaths[2]

End point description:

An AE was defined as any new unfavorable/unintended signs/symptoms (including abnormal laboratory findings), or diagnosis or worsening of a pre-existing condition, which occurred following screening and at any point up to the post-treatment safety follow-up visit, which may or may not be related to the IMP. An AE was considered serious if it: (1) was fatal; (2) was life-threatening; (3) required inpatient hospitalization or prolonged existing hospitalization; (4) was persistently or significantly disabling or incapacitating; (5) was a congenital anomaly/birth defect; or (6) was a medically significant event that, based upon appropriate medical judgment, may have jeopardized the subject and may have required medical or surgical intervention to prevent one of the outcomes listed above. Analysis was performed in OLE Safety Analysis Set population.

End point type	Primary

End point timeframe:

OLE: up to approximately 4 years

Notes:

[2] - 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: Only descriptive statistics was planned for this endpoint.

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects				
Treatment-Related TEAEs	80	60		
TEAEs Leading to Permanent Discontinuation	11	7		
Serious TEAEs	38	18		
Deaths	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: OLE: Number of Subjects With TEAEs by Severity

End point title	OLE: Number of Subjects With TEAEs by Severity[3]

End point description:

An AE was defined as any new unfavorable/unintended signs/symptoms (including abnormal laboratory findings), or diagnosis or worsening of a pre-existing condition, which occurred following screening and at any point up to the post-treatment safety follow-up visit, which may or may not be related to the IMP. Analysis was performed in OLE Safety Analysis Set population.

End point type	Primary

End point timeframe:

OLE: up to approximately 4 years

Notes:

[3] - 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: Only descriptive statistics was planned for this endpoint.

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects				
Mild	35	16		
Moderate	63	48		
Severe	19	11		

Statistical analyses

No statistical analyses for this end point

Secondary: DBP: Number of Subjects Considered Treatment Responders During the DBP Treatment Period (Maintenance and Titration)

End point title	DBP: Number of Subjects Considered Treatment Responders During the DBP Treatment Period (Maintenance and Titration)

End point description:

Treatment responders were defined as those subjects with a ≥ 50% reduction in TSC-associated seizure frequency. TSC-associated seizures included: focal motor seizures without impairment of consciousness or awareness (Type 1 focal motor); focal seizures with impairment of consciousness or awareness (Type 2 focal); focal seizures evolving to bilateral generalized convulsive seizures (Type 3 focal); and tonic-clonic, tonic, clonic, or atonic seizures that were countable. Subjects who withdrew from the trial during the treatment period were considered non-responders. ITT Analysis Set population.

End point type	Secondary

End point timeframe:

DBP: Baseline; up to Week 16

End point values	DBP: GWP42003-P 25 mg/kg/Day	DBP: GWP42003-P 50 mg/kg/Day	DBP: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	73	76	
Units: Subjects				
Responders	27	29	17	
Non-responders	48	44	59	

Statistical analyses

Statistical analysis title	GWP42003-P 25 mg/kg/Day, Placebo
Comparison groups	DBP: GWP42003-P 25 mg/kg/Day v DBP: Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0692 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	4

Notes:

[4] - The p-value was calculated from a Cochran-Mantel-Haenszel test stratified by age group (1-6, 7-11, 12-17 and 18-65 years).

Statistical analysis title	GWP42003-P 50 mg/kg/Day, Placebo

Comparison groups	DBP: Placebo v DBP: GWP42003-P 50 mg/kg/Day
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0245 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	4.67

Notes:

[5] - The p-value was calculated from a Cochran-Mantel-Haenszel test stratified by age group (1-6, 7-11, 12-17 and 18-65 years).

Secondary: DBP: Change From Baseline in the Caregiver Global Impression of Change (CGIC) or Subject Global Impression of Change (PGIC) Score

End point title	DBP: Change From Baseline in the Caregiver Global Impression of Change (CGIC) or Subject Global Impression of Change (PGIC) Score

End point description:

Combined caregiver and subject summary uses either caregiver or subject version if only one version was completed, or caregiver version if both caregiver and subject versions were completed. CGIC comprised following question, to be rated on a 7-point scale (1, Very Much Improved; 2, Much Improved; 3, Slightly Improved; 4, No Change; 5, Slightly Worse; 6, Much Worse; 7, Very Much Worse): "Since your child started treatment, please assess the status of your child's overall condition (comparing their condition now to their condition before treatment)." SGIC comprised the following question, to be rated on a 7-point scale (1, Very Much Improved; 2, Much Improved; 3, Slightly Improved; 4, No Change; 5, Slightly Worse; 6, Much Worse; 7, Very Much Worse): "Since you started treatment, please assess the status of your overall condition (comparing your condition now to your condition before treatment)." ITT Analysis Set. Here ''n" signifies subjects analysed in each arm.

End point type	Secondary

End point timeframe:

DBP: Baseline; up to Week 16

End point values	DBP: GWP42003-P 25 mg/kg/Day	DBP: GWP42003-P 50 mg/kg/Day	DBP: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	73	76	
Units: score on a scale				
arithmetic mean (standard deviation)				
Caregiver (n=66,66,72)	3.0 (± 1.34)	3.1 (± 1.40)	3.5 (± 0.93)	
Combined Caregiver and Subject (n=70,69,66)	3.0 (± 1.35)	3.2 (± 1.45)	3.5 (± 0.96)	
Subject (n=6,4,4)	3.3 (± 1.51)	4.5 (± 1.73)	2.8 (± 1.26)	

Statistical analyses

Statistical analysis title	GWP42003-P 25 mg/kg/Day, Placebo
Comparison groups	DBP: GWP42003-P 25 mg/kg/Day v DBP: Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0074 [6]
Method	nominal
Parameter estimate	Ordinal logistic regression
Point estimate	2.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.24
upper limit	4.07

Notes:

[6] - The global impression of change was analyzed using an ordinal logistic regression model with treatment group as a fixed factor.

Statistical analysis title	GWP42003-P 50 mg/kg/Day, Placebo
Comparison groups	DBP: Placebo v DBP: GWP42003-P 50 mg/kg/Day
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058 [7]
Method	nominal
Parameter estimate	Ordinal logistic regression
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	3.2

Notes:

[7] - The global impression of change was analyzed using an ordinal logistic regression model with treatment group as a fixed factor.

Secondary: DBP: Percent Change From Baseline in Total Seizures During the Treatment Period (Maintenance and Titration)

End point title	DBP: Percent Change From Baseline in Total Seizures During the Treatment Period (Maintenance and Titration)

End point description:

Total seizures included all seizure types combined. Percent change from Baseline was calculated as the (post-Baseline value minus the Baseline value) divided by the Baseline value x 100. ITT Analysis Set population.

End point type	Secondary

End point timeframe:

DBP: Baseline; up to Week 16

End point values	DBP: GWP42003-P 25 mg/kg/Day	DBP: GWP42003-P 50 mg/kg/Day	DBP: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	73	76	
Units: Percent change				
arithmetic mean (standard deviation)	-34.71 (± 46.150)	-35.14 (± 42.530)	-19.63 (± 35.137)	

Statistical analyses

Statistical analysis title	GWP42003-P 25 mg/kg/Day, Placebo
Comparison groups	DBP: GWP42003-P 25 mg/kg/Day v DBP: Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0013
Method	Mixed model analysis
Parameter estimate	Treatment ratio
Point estimate	0.709
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.576
upper limit	0.873

Statistical analysis title	GWP42003-P 50 mg/kg/Day, Placebo
Comparison groups	DBP: Placebo v DBP: GWP42003-P 50 mg/kg/Day
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0018
Method	Mixed model analysis
Parameter estimate	Treatment ratio
Point estimate	0.716
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.582
upper limit	0.882

Secondary: DBP: Number of Subjects With Any Severe Treatment-emergent Adverse Events (TEAE)

End point title	DBP: Number of Subjects With Any Severe Treatment-emergent Adverse Events (TEAE)

End point description:

A TEAE was defined as an AE with a start date on or after the first dose of IMP during the DBP up to and including the date of first dose of the OLE Phase (OLE Day 1). Safety Analysis Set: all subjects randomized to treatment who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

DBP: Up to approximately Week 22

End point values	DBP: GWP42003-P 25 mg/kg/Day	DBP: GWP42003-P 50 mg/kg/Day	DBP: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	73	76	
Units: Subjects	7	9	1	

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Percent Change from Baseline in the TSC-associated Seizures During the OLE Treatment Period

End point title	OLE: Percent Change from Baseline in the TSC-associated Seizures During the OLE Treatment Period

End point description:

TSC-associated seizures include: focal motor seizures without impairment of consciousness or awareness; focal seizures with impairment of consciousness or awareness; focal seizures evolving to bilateral generalized convulsive seizures and tonic-clonic, tonic, clonic or atonic seizures. OLE last 12 weeks was defined as all available data from 12 weeks prior to the earliest of the OLE completion date or the last call to IVRS. Seizure scores were averaged per 28 days. Percent change from Baseline was calculated as the (post-Baseline value minus the Baseline value) divided by the Baseline value x 100. A negative change from baseline indicates improvement. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE: Baseline, OLE Treatment Period (up to 209 weeks), Last 12 weeks of study treatment

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Frequency of Seizure				
median (inter-quartile range (Q1-Q3))				
Last 12 Weeks	-62.95 (-95.26 to -12.44)	-58.53 (-82.01 to -9.58)		

OLE Treatment Period	-55.66 (-86.47 to -12.33)	-46.76 (-78.17 to -15.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects Considered Treatment Responders During the OLE Treatment Period

End point title	OLE: Number of Subjects Considered Treatment Responders During the OLE Treatment Period

End point description:

Treatment responders were defined as those subjects with a ≥ 50% reduction from baseline in TSC-associated seizure frequency, during the treatment period, for subjects who had not withdrawn from the trial during the treatment period. TSC-associated seizures included: focal motor seizures without impairment of consciousness or awareness (Type 1 focal motor); focal seizures with impairment of consciousness or awareness (Type 2 focal); focal seizures evolving to bilateral generalized convulsive seizures (Type 3 focal); and tonic-clonic, tonic, clonic, or atonic seizures that were countable. Subjects who withdrew from the trial during the treatment period were considered non-responders. OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE: Baseline; up to 209 weeks

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects				
≥ 25% reduction: Yes	86	53		
≥ 25% reduction: No	38	22		
≥ 50% reduction: Yes	70	36		
≥ 50% reduction: No	54	39		
≥ 75% reduction: Yes	43	22		
≥ 75% reduction: No	81	53		
100% reduction: Yes	5	0		
100% reduction: No	119	75		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects Experiencing a Worsening, no change, or

improvements in TSC-associated seizure frequency	
End point title	OLE: Number of Subjects Experiencing a Worsening, no change, or improvements in TSC-associated seizure frequency

End point description:

Treatment responders were defined as those subjects with a ≥ 50% reduction from baseline in TSC-associated seizure frequency, during the treatment period, for subjects who had not withdrawn from the trial during the treatment period. Worsening was categorized as experienced a > 25% worsening; experienced −25% to +25% no change; experienced 25% to 50% improvement; experienced 50% to 75% improvement; and experienced > 75% improvement. TSC-associated seizures included: focal motor seizures without impairment of consciousness or awareness (Type 1 focal motor); focal seizures with impairment of consciousness or awareness (Type 2 focal); focal seizures evolving to bilateral generalized convulsive seizures (Type 3 focal); and tonic-clonic, tonic, clonic, or atonic seizures that were countable. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE treatment period (Approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects				
> 25% worsening	8	7		
−25 to +25% no change	24	15		
25 to 50% improvement	16	17		
50 to 75% improvement	27	14		
> 75% improvement	43	22		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Percent Change from Baseline in Total Seizure Frequency	
End point title	OLE: Percent Change from Baseline in Total Seizure Frequency

End point description:

Total seizures include all seizure types i.e. combination of TSC-associated and other seizures. Percent change from Baseline was calculated as the (post-Baseline value minus the Baseline value) divided by the Baseline value x 100. A negative change from baseline indicates improvement. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE: Baseline; OLE treatment period (up to 209 weeks)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Percentage change				
median (inter-quartile range (Q1-Q3))	-55.18 (-84.21 to -11.95)	-46.76 (-76.22 to -19.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in Number of TSC-associated Seizure-Free Days

End point title	OLE: Change from Baseline in Number of TSC-associated Seizure-Free Days

End point description:

Seizure information was collected daily during the double-blind phase but weekly during the OLE phase. Therefore, the change in number of TSC-associated-seizure-free days could not be calculated for the OLE phase.

End point type	Secondary

End point timeframe:

OLE: Baseline; OLE treatment period (up to approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: Days				
number (not applicable)				

Notes:

[8] - Change in number of TSC-associated-seizure-free days could not be calculated.

[9] - Change in number of TSC-associated-seizure-free days could not be calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change From Baseline in the Caregiver Global Impression of Change (CGIC) or Participant Global Impression of Change (PGIC) Score

End point title	OLE: Change From Baseline in the Caregiver Global Impression of Change (CGIC) or Participant Global Impression of Change (PGIC) Score

End point description:

The combined caregiver and participant summary uses either the caregiver or participant version if only

one version was completed, or the caregiver version if both caregiver and participant versions were completed. The CGIC comprised the following question, to be rated on a 7-point scale (1, Very Much Improved; 2, Much Improved; 3, Slightly Improved; 4, No Change; 5, Slightly Worse; 6, Much Worse; 7, Very Much Worse): "Since your child started treatment, please assess the status of your child's overall condition (comparing their condition now to their condition before treatment)." The SGIC comprised the following question, to be rated on a 7-point scale (1, Very Much Improved; 2, Much Improved; 3, Slightly Improved; 4, No Change; 5, Slightly Worse; 6, Much Worse; 7, Very Much Worse): "Since you started treatment, please assess the status of your overall condition (comparing your condition now to your condition before treatment)." Analysis was performed in OLE Safety Analysis Set.

End point type	Secondary

End point timeframe:

OLE: Baseline; OLE End of Treatment (up to 209 weeks)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: score on a scale				
arithmetic mean (standard deviation)				
Caregiver (n=39,25)	3.2 (± 1.58)	3.4 (± 1.12)		
Subject (n=3,3)	4.0 (± 0.0)	2.7 (± 1.53)		
Combined Caregiver and Subject (n=40,28)	3.2 (± 1.56)	3.3 (± 1.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in Physician Global Impression of Change (PGIC) Score

End point title	OLE: Change from Baseline in Physician Global Impression of Change (PGIC) Score

End point description:

The PGIC comprised the following question, rated on a seven-point scale: “Very Much Improved”; “Much Improved”; “Slightly Improved”; “No Change”; “Slightly Worse”; “Much Worse”; “Very Much Worse”, which assess the change in the subject's general functional abilities. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed in OLE Safety Analysis Set population. Here 'N', signifies the number of subjects evaluable at the specified time point for this outcome measure.

End point type	Secondary

End point timeframe:

OLE: Baseline; OLE Last Visit (up to approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	72		
Units: Score on a scale				
arithmetic mean (standard deviation)	2.8 (± 1.22)	3.0 (± 1.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in Quality of Life in Childhood Epilepsy (QOLCE) Score

End point title	OLE: Change from Baseline in Quality of Life in Childhood Epilepsy (QOLCE) Score

End point description:

Quality of life (QOL) was measured using the QOLCE questionnaire which has good construct validity, internal consistency, test-retest reliability, and sensitivity to epilepsy severity. Each subscale consists of a number of questions in addition to a 'distress' item. The raw score for each question and the 'distress' item was converted to a 0-100 score. A final subscale weighted score was calculated where higher scores reflect better quality of life; lower ones, worse quality of life. The overall QOL score was calculated by taking the mean of the subscale scores. Baseline was defined as Day 1 of the DBP. Analysis was performed in OLE Safety Analysis Set population. Here 'N', signifies the number of subjects evaluable at the specified time point for this outcome measure.

End point type	Secondary

End point timeframe:

OLE: Baseline, OLE treatment period (up to approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	14		
Units: Score on a scale				
arithmetic mean (standard deviation)	-3.4 (± 13.90)	-5.6 (± 13.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in Quality of Life in Epilepsy (QOLIE-31-P) Score

End point title	OLE: Change from Baseline in Quality of Life in Epilepsy (QOLIE-31-P) Score

End point description:

Quality of life (QOL) was measured using the QOLIE-31-P questionnaire. Each subscale consists of a number of questions in addition to a 'distress' item. The raw score for each question and the 'distress' item was converted to a 0-100 score. A final subscale weighted score was calculated where higher scores reflect better quality of life; lower ones, worse quality of life. The overall quality of life score was calculated by taking the mean of the subscale scores. The total score was calculated as: (Sum of all subscale weighted scores ÷ Sum of all subscale 'distress' item converted scores) × 100. Baseline was defined as Day 1 of the double-blind phase. Analysis was performed in OLE Safety Analysis Set population. Here 'N', signifies the number of subjects evaluable at the specified time point for this outcome measure.

End point type	Secondary

End point timeframe:

OLE: Baseline; OLE End of Treatment (up to approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: score on a scale				
arithmetic mean (standard deviation)	-14.8 (± 20.60)	-1.8 (± 13.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in Other Seizure Frequency

End point title	OLE: Change from Baseline in Other Seizure Frequency

End point description:

Other seizures include absence, myoclonic, partial sensory seizures, and infantile or epileptic spasms. Baseline period includes all data prior to Day 1 of the double-blind phase. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. A negative change from baseline indicates improvement. Analysis was performed in OLE Safety Analysis Set population. Here 'N', signifies the number of subjects evaluable at the specified time point for this outcome measure.

End point type	Secondary

End point timeframe:

OLE: Baseline; OLE treatment period (Approx 209 weeks)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	15		
Units: Percentage change				

median (inter-quartile range (Q1-Q3))	-84.43 (-100.0 to -59.61)	-99.0 (-100.0 to -47.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Change from Baseline in Serum Insulin-like Growth Factor-1 (IGF-1) levels

End point title	OLE: Change from Baseline in Serum Insulin-like Growth Factor-1 (IGF-1) levels

End point description:

Serum IGF-1 concentrations were determined. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed in OLE Safety Analysis Set population. Here 'N', signifies the number of subjects evaluable at the specified time point for this outcome measure.

End point type	Secondary

End point timeframe:

OLE: Baseline; OLE End of Treatment (up to approximately 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	17		
Units: nanomole(s)/litre				
arithmetic mean (standard deviation)	-0.54 (± 9.069)	-1.0 (± 9.057)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects with Indicated Tanner stages

End point title	OLE: Number of Subjects with Indicated Tanner stages

End point description:

For all adolescent subjects (10-17 years of age), the onset and progression of pubertal changes were assessed by Tanner staging. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE treatment period (up to 209 weeks)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects				
Tanner Stage 1	0	2		
Tanner Stage 2	7	1		
Tanner Stage 3	3	1		
Tanner Stage 4	2	2		
Tanner Stage 5	4	2		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects with Suicidal Ideation and Behavior

End point title	OLE: Number of Subjects with Suicidal Ideation and Behavior

End point description:

Suicidality was assessed either by using the C-SSRS/Children's C-SSRS or, in subjects with profound cognitive impairment, by the investigator's clinical judgment. Common items from the Adult and Child C-SSRS questionnaires were combined for this summary. Suicidal Ideation: Wish to be dead; Non-specific active suicidal thoughts; Active suicidal ideation with any methods (not plan) without intent to act; Active suicidal ideation with some intent to act, without specific plan; Active suicidal ideation with specific plan and intent. Suicidal Behavior: Actual attempt; Interrupted attempt; Aborted attempt; Preparatory acts or behavior; Suicidal behavior; Completed suicide. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE treatment period (up to approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects				
Suicidal Ideation	0	0		
Suicidal Behavior	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects with Clinically Significant Laboratory Abnormalities

End point title	OLE: Number of Subjects with Clinically Significant Laboratory Abnormalities

End point description:

Blood and urine samples were collected at the scheduled visits for hematology, biochemistry, and urinalysis. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE treatment period (up to approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects Who Reported Hospitalizations

End point title	OLE: Number of Subjects Who Reported Hospitalizations

End point description:

The number of inpatient hospitalizations due to epilepsy were reported. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE treatment period (Approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects	28	10		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects with Clinically Significant 12-Lead Electrocardiogram (ECG)

End point title	OLE: Number of Subjects with Clinically Significant 12-Lead Electrocardiogram (ECG)

End point description:

12-lead ECG recordings were performed after 5 minutes in supine position. A physician reviewed the ECG and any abnormal findings considered to indicate significant medical history or AEs were recorded appropriately on the CRF. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE treatment period (up to approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects with Drug Abuse Based on Study Medication Use and Behavior Survey

End point title	OLE: Number of Subjects with Drug Abuse Based on Study Medication Use and Behavior Survey

End point description:

All subjects/caregivers were interviewed and a Study Medication Use and Behavior Survey was completed which consisted of 17 questions regarding the use of the IMP. Of the 17 questions, 14 were marked unanimously as ‘never,’ ‘no desire,’ or ‘not at all’ including all those relating to routes of administration and diversion. For the remaining 3 questions, relating to drug dosage, dose impact, withdrawal syndrome, and desired use, the number of responses which were marked as anything other than ‘never,’ ‘no,’ or ‘not at all’. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE treatment period (Approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects				
Used more than the maximum daily dose	0	2		
Took additional dose to improve relief of seizures	0	1		
Took additional dose to treat other symptoms	0	1		
Develop new emotional or psychological issues	3	1		
Expressed concern over medication use	8	5		
Interference with normal activities	7	3		
Lead to problems with the police	1	0		
Had to be less honest to anybody about drug use	1	0		
How often stopped taking study medications	1	3		
Sign and symptoms consistent to withdrawal symptom	1	1		
Took additional study medication by accident	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Female Subjects with Abnormal Changes Related to Menstrual Cycle

End point title	OLE: Number of Female Subjects with Abnormal Changes Related to Menstrual Cycle

End point description:

Caregivers of female subjects were asked if the subject was menstruating and details were recorded. Analysis was performed in OLE Safety Analysis Set population. Here, 'N' signifies the number of female subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

OLE treatment period (up to 209 weeks)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	30		
Units: Subjects				
Changes in Menstrual Cycle	1	1		
Abnormalities Related to Menstrual Cycle	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects with Clinically Significant Changes in Indicated Physical Examination Parameters

End point title	OLE: Number of Subjects with Clinically Significant Changes in Indicated Physical Examination Parameters

End point description:

A physical examination was performed at the screening to ensure that the subject was eligible to enter the trial. Physical examinations included height and body weight measurements. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE treatment period (up to approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects				
Weight <= -7 %	6	4		
Weight >= 7 %	16	8		
Height	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE: Number of Subjects with Clinically Significant Changes in Indicated Vital Signs

End point title	OLE: Number of Subjects with Clinically Significant Changes in Indicated Vital Signs

End point description:

Vital sign measurements included body temperature, pulse rate, respiration rate, including blood pressure taken in a sitting position at rest for 5 minutes. Analysis was performed in OLE Safety Analysis Set population.

End point type	Secondary

End point timeframe:

OLE treatment period (up to approx 4 years)

End point values	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	75		
Units: Subjects				
Sitting Systolic Blood Pressure < -20 mmHg	3	3		
Sitting Systolic Blood Pressure > 20 mmHg	2	2		
Sitting Diastolic Blood Pressure < -10 mmHg	7	2		
Sitting Diastolic Blood Pressure > 10 mmHg	8	9		
Pulse Rate < -10 beats/min	13	7		
Pulse Rate > 10 beats/min	9	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

DBP: From the start of treatment up to Week 22; OLE: From the start of treatment up to 4 years.

Adverse event reporting additional description:

Safety Analysis Set, comprised of subjects randomized to treatment who received at least 1 dose of IMP. Treatment-emergent adverse events were defined as adverse events with a start date on or after the first dose of IMP throughout the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	DBP: GWP42003-P 25 mg/kg/Day

Reporting group description:

Subjects were randomized to receive GWP42003-P 25 milligrams per kilogram per day (mg/kg/day) orally twice daily (morning and evening administration). Subjects completed a 4-week dose-escalation period, titrating up to their assigned dose, before continuing on a stable dose of blinded GWP42003-P for 12 weeks.

Reporting group title	DBP: GWP42003-P 50 mg/kg/Day

Reporting group description:

Subjects were randomized to receive GWP42003-P 50 mg/kg/day orally twice daily (morning and evening administration). Subjects completed a 4-week dose escalation period, titrating up to their assigned dose, before continuing on a stable dose of blinded GWP42003-P for 12 weeks.

Reporting group title	DBP: Placebo

Reporting group description:

Subjects were randomized to receive placebo matched to GWP42003-P orally twice daily (morning and evening administration) for 16 weeks.

Reporting group title	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)

Reporting group description:

Subjects who completed the DBP entered a 2-week blinded transition prior to the OLE. During the transition, open-label IMP was titrated up to 25 mg/kg/day whilst blinded IMP was simultaneously tapered down to zero to accommodate those subjects who had been randomized to placebo during the double-blind phase of the study. Transition from the DBP to the OLE were as follows: Subjects receiving placebo during the DBP were titrated up to receive 25 mg/kg/day in OLE phase, subjects receiving 25 mg/kg/day of GWP42003-P during the DBP continued to receive 25 mg/kg/day in OLE phase, subjects receiving 50 mg/kg/day of GWP42003-P during the DBP were tapered (10% per day for 5 days) to receive 25 mg/kg/day of GWP42003-P during OLE. All subjects completed the transition and entered the OLE taking 25 mg/kg/day GWP42003-P.

Reporting group title	OLE: Placebo (DBP) then GWP42003-P (OLE)

Reporting group description:

Subjects who completed the DBP entered a 2-week blinded transition prior to the OLE. During the transition, open-label IMP was titrated up to 25 mg/kg/day whilst blinded IMP was simultaneously tapered down to zero to accommodate those subjects who had been randomized to placebo during the double-blind phase of the study. Transition from the DBP to the OLE were as follows: Subjects receiving placebo during the DBP were titrated up to receive 25 mg/kg/day in OLE phase, subjects receiving 25 mg/kg/day of GWP42003-P during the DBP continued to receive 25 mg/kg/day in OLE phase, subjects receiving 50 mg/kg/day of GWP42003-P during the DBP were tapered (10% per day for 5 days) to receive 25 mg/kg/day of GWP42003-P during OLE. All subjects completed the transition and entered the OLE taking 25 mg/kg/day GWP42003-P.

Serious adverse events	DBP: GWP42003-P 25 mg/kg/Day	DBP: GWP42003-P 50 mg/kg/Day	DBP: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 75 (21.33%)	10 / 73 (13.70%)	2 / 76 (2.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Kidney angiomyolipoma			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue inflammation			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Type IV hypersensitivity reaction			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Alcohol use			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 75 (2.67%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anticonvulsant drug level increased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 75 (2.67%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Astrovirus test positive			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Eosinophil count increased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza A virus test positive			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigation			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus test positive			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sapovirus test positive			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			

subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Cardiopulmonary failure			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Change in seizure presentation			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epileptic encephalopathy			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postictal state			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sedation			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure cluster			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental caries			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Liver injury			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash erythematous			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash macular			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenoiditis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovirus infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis astroviral			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis viral			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective myositis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid intake reduced			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OLE: GWP42003-P	OLE: Placebo (DBP)	

	(DBP) then GWP42003-P (OLE)	then GWP42003-P (OLE)	
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 124 (30.65%)	18 / 75 (24.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Kidney angiomyolipoma			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue inflammation			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Type IV hypersensitivity reaction			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Alcohol use			

subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (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	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (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	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	2 / 124 (1.61%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anticonvulsant drug level increased			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Astrovirus test positive			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Eosinophil count increased			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza A virus test positive			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigation			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus test positive			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sapovirus test positive			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			

subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	4 / 124 (3.23%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Cardiopulmonary failure			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Change in seizure presentation			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epileptic encephalopathy			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			

subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postictal state			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sedation			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	12 / 124 (9.68%)	4 / 75 (5.33%)	
occurrences causally related to treatment / all	0 / 14	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure cluster			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	9 / 124 (7.26%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	2 / 20	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Liver injury			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash erythematous			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash macular			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (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			
Adenoiditis			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	2 / 124 (1.61%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovirus infection			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis astroviral			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis viral			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site infection			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective myositis			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	5 / 124 (4.03%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 124 (0.00%)	16 / 75 (21.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			

subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis streptococcal			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 124 (3.23%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (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			

subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid intake reduced			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	DBP: GWP42003-P 25 mg/kg/Day	DBP: GWP42003-P 50 mg/kg/Day	DBP: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 75 (88.00%)	71 / 73 (97.26%)	71 / 76 (93.42%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 75 (2.67%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 75 (4.00%)	4 / 73 (5.48%)	1 / 76 (1.32%)
occurrences (all)	3	4	1
Feeling abnormal			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	4 / 75 (5.33%)	3 / 73 (4.11%)	2 / 76 (2.63%)
occurrences (all)	4	3	2
Pyrexia			
subjects affected / exposed	14 / 75 (18.67%)	12 / 73 (16.44%)	6 / 76 (7.89%)
occurrences (all)	23	14	6
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	1 / 75 (1.33%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences (all)	1	2	0
Cough			
subjects affected / exposed	8 / 75 (10.67%)	3 / 73 (4.11%)	5 / 76 (6.58%)
occurrences (all)	8	3	5
Epistaxis			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	2 / 76 (2.63%)
occurrences (all)	1	1	2
Nasal congestion			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	3 / 76 (3.95%)
occurrences (all)	0	0	3
Oropharyngeal pain			
subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	1 / 76 (1.32%)
occurrences (all)	0	2	1
Pulmonary congestion			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Respiration abnormal			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	3 / 75 (4.00%)	3 / 73 (4.11%)	0 / 76 (0.00%)
occurrences (all)	3	3	0
Throat irritation			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	2	0	0
Wheezing			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 75 (1.33%)	2 / 73 (2.74%)	1 / 76 (1.32%)
occurrences (all)	1	2	1
Affect lability			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Aggression			
subjects affected / exposed	2 / 75 (2.67%)	2 / 73 (2.74%)	3 / 76 (3.95%)
occurrences (all)	3	3	3
Agitation			
subjects affected / exposed	2 / 75 (2.67%)	2 / 73 (2.74%)	3 / 76 (3.95%)
occurrences (all)	2	2	3
Anxiety			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	2	0	1
Insomnia			
subjects affected / exposed	3 / 75 (4.00%)	2 / 73 (2.74%)	5 / 76 (6.58%)
occurrences (all)	4	2	6
Intentional self-injury			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	4 / 75 (5.33%)	5 / 73 (6.85%)	4 / 76 (5.26%)
occurrences (all)	4	6	5
Mental status changes			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	0	1	0
Panic attack			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	2	0	0
Sleep disorder			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	2 / 76 (2.63%)
occurrences (all)	0	1	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 75 (9.33%)	14 / 73 (19.18%)	0 / 76 (0.00%)
occurrences (all)	7	16	0

Anticonvulsant drug level increased			
subjects affected / exposed	1 / 75 (1.33%)	2 / 73 (2.74%)	1 / 76 (1.32%)
occurrences (all)	1	2	1
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 75 (8.00%)	12 / 73 (16.44%)	0 / 76 (0.00%)
occurrences (all)	6	13	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	1	2	0
Blood iron decreased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Blood prolactin increased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	3 / 76 (3.95%)
occurrences (all)	1	0	3
Blood urea increased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	2 / 76 (2.63%)
occurrences (all)	0	0	2
Eosinophil count increased			
subjects affected / exposed	4 / 75 (5.33%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	4	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	12 / 75 (16.00%)	10 / 73 (13.70%)	0 / 76 (0.00%)
occurrences (all)	12	11	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 75 (0.00%)	3 / 73 (4.11%)	0 / 76 (0.00%)
occurrences (all)	0	3	0
International normalised ratio increased			
subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences (all)	0	3	0
Liver function test increased			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	3 / 75 (4.00%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences (all)	3	2	0
Prothrombin time prolonged			
subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	5 / 75 (6.67%)	6 / 73 (8.22%)	0 / 76 (0.00%)
occurrences (all)	5	6	0
Weight increased			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	2 / 76 (2.63%)
occurrences (all)	1	0	2
White blood cell count decreased			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	0	1	0
White blood cell count increased			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	4 / 76 (5.26%)
occurrences (all)	1	1	5
Eye contusion			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	0	1	0
Face injury			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	2 / 75 (2.67%)	4 / 73 (5.48%)	5 / 76 (6.58%)
occurrences (all)	2	4	7
Foot fracture			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	1 / 76 (1.32%)
occurrences (all)	0	1	2
Laceration			
subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences (all)	0	2	0
Ligament sprain			
subjects affected / exposed	1 / 75 (1.33%)	2 / 73 (2.74%)	1 / 76 (1.32%)
occurrences (all)	1	2	1
Lip injury			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	1 / 76 (1.32%)
occurrences (all)	1	1	1
Tooth fracture			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Ataxia			
subjects affected / exposed	3 / 75 (4.00%)	2 / 73 (2.74%)	2 / 76 (2.63%)
occurrences (all)	5	2	2
Balance disorder			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	2 / 76 (2.63%)
occurrences (all)	0	0	4

Dizziness			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	3 / 76 (3.95%)
occurrences (all)	6	0	3
Drooling			
subjects affected / exposed	1 / 75 (1.33%)	2 / 73 (2.74%)	2 / 76 (2.63%)
occurrences (all)	1	2	2
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	4 / 75 (5.33%)	2 / 73 (2.74%)	4 / 76 (5.26%)
occurrences (all)	8	6	5
Hypersomnia			
subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences (all)	0	2	0
Hypokinesia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	4 / 75 (5.33%)	3 / 73 (4.11%)	5 / 76 (6.58%)
occurrences (all)	4	3	5
Psychomotor hyperactivity			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
Sedation			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1
Seizure			
subjects affected / exposed	4 / 75 (5.33%)	6 / 73 (8.22%)	5 / 76 (6.58%)
occurrences (all)	4	7	6
Somnolence			
subjects affected / exposed	10 / 75 (13.33%)	19 / 73 (26.03%)	7 / 76 (9.21%)
occurrences (all)	10	21	8
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	5 / 75 (6.67%)	3 / 73 (4.11%)	1 / 76 (1.32%)
occurrences (all)	5	3	1
Eosinophilia			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	1	1	0
Increased tendency to bruise			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	2 / 76 (2.63%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 75 (2.67%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	1	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 75 (0.00%)	3 / 73 (4.11%)	1 / 76 (1.32%)
occurrences (all)	0	3	1
Constipation			
subjects affected / exposed	8 / 75 (10.67%)	5 / 73 (6.85%)	6 / 76 (7.89%)
occurrences (all)	9	7	6
Diarrhoea			
subjects affected / exposed	23 / 75 (30.67%)	40 / 73 (54.79%)	19 / 76 (25.00%)
occurrences (all)	36	54	26
Frequent bowel movements			
subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences (all)	0	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	0	1	0
Nausea			

subjects affected / exposed	6 / 75 (8.00%)	2 / 73 (2.74%)	2 / 76 (2.63%)
occurrences (all)	8	2	2
Retching			
subjects affected / exposed	2 / 75 (2.67%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	3	1	0
Salivary hypersecretion			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	12 / 75 (16.00%)	13 / 73 (17.81%)	7 / 76 (9.21%)
occurrences (all)	20	22	13
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
Dermatitis diaper			
subjects affected / exposed	2 / 75 (2.67%)	1 / 73 (1.37%)	1 / 76 (1.32%)
occurrences (all)	2	1	1
Erythema			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	3 / 75 (4.00%)	7 / 73 (9.59%)	2 / 76 (2.63%)
occurrences (all)	3	7	3
Rash maculo-papular			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	0	1	0

Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 75 (2.67%)	1 / 73 (1.37%)	1 / 76 (1.32%)
occurrences (all)	2	1	1
Conjunctivitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	2	0	0
Croup infectious			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	2
Ear infection			
subjects affected / exposed	2 / 75 (2.67%)	4 / 73 (5.48%)	0 / 76 (0.00%)
occurrences (all)	2	4	0
Gastroenteritis			
subjects affected / exposed	3 / 75 (4.00%)	2 / 73 (2.74%)	2 / 76 (2.63%)
occurrences (all)	3	2	3
Gastroenteritis viral			
subjects affected / exposed	1 / 75 (1.33%)	3 / 73 (4.11%)	3 / 76 (3.95%)
occurrences (all)	1	3	4
Influenza			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	11 / 75 (14.67%)	11 / 73 (15.07%)	12 / 76 (15.79%)
occurrences (all)	13	12	16
Otitis media			
subjects affected / exposed	2 / 75 (2.67%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	3	1	0

Pharyngitis			
subjects affected / exposed	1 / 75 (1.33%)	2 / 73 (2.74%)	2 / 76 (2.63%)
occurrences (all)	1	2	2
Pharyngitis streptococcal			
subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	1 / 76 (1.32%)
occurrences (all)	0	2	1
Pneumonia			
subjects affected / exposed	2 / 75 (2.67%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences (all)	2	2	0
Respiratory tract infection			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	2 / 76 (2.63%)
occurrences (all)	2	0	2
Rhinitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1
Tonsillitis			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	2	0	1
Upper respiratory tract infection			
subjects affected / exposed	7 / 75 (9.33%)	7 / 73 (9.59%)	10 / 76 (13.16%)
occurrences (all)	8	8	11
Urinary tract infection			
subjects affected / exposed	4 / 75 (5.33%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	4	2	0
Viral infection			
subjects affected / exposed	3 / 75 (4.00%)	0 / 73 (0.00%)	2 / 76 (2.63%)
occurrences (all)	3	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	15 / 75 (20.00%)	17 / 73 (23.29%)	9 / 76 (11.84%)
occurrences (all)	16	19	9
Dehydration			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	0 / 76 (0.00%)
occurrences (all)	1	1	0
Diet refusal			
subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	0 / 76 (0.00%)
occurrences (all)	0	2	0
Increased appetite			
subjects affected / exposed	3 / 75 (4.00%)	3 / 73 (4.11%)	5 / 76 (6.58%)
occurrences (all)	3	3	5

Non-serious adverse events	OLE: GWP42003-P (DBP) then GWP42003-P (OLE)	OLE: Placebo (DBP) then GWP42003-P (OLE)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	115 / 124 (92.74%)	75 / 75 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 124 (1.61%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 124 (5.65%)	10 / 75 (13.33%)	
occurrences (all)	7	13	
Feeling abnormal			
subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	3	
Gait disturbance			
subjects affected / exposed	4 / 124 (3.23%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Pyrexia			

subjects affected / exposed	32 / 124 (25.81%)	15 / 75 (20.00%)	
occurrences (all)	66	27	
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Seasonal allergy			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 124 (1.61%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Cough			
subjects affected / exposed	12 / 124 (9.68%)	13 / 75 (17.33%)	
occurrences (all)	26	14	
Epistaxis			
subjects affected / exposed	2 / 124 (1.61%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
Nasal congestion			
subjects affected / exposed	7 / 124 (5.65%)	5 / 75 (6.67%)	
occurrences (all)	8	5	
Oropharyngeal pain			
subjects affected / exposed	6 / 124 (4.84%)	5 / 75 (6.67%)	
occurrences (all)	7	6	
Pulmonary congestion			
subjects affected / exposed	3 / 124 (2.42%)	1 / 75 (1.33%)	
occurrences (all)	3	1	
Respiration abnormal			
subjects affected / exposed	4 / 124 (3.23%)	0 / 75 (0.00%)	
occurrences (all)	6	0	
Rhinorrhoea			
subjects affected / exposed	6 / 124 (4.84%)	4 / 75 (5.33%)	
occurrences (all)	6	5	
Throat irritation			

subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	6 / 124 (4.84%)	5 / 75 (6.67%)	
occurrences (all)	7	6	
Affect lability			
subjects affected / exposed	3 / 124 (2.42%)	1 / 75 (1.33%)	
occurrences (all)	3	2	
Aggression			
subjects affected / exposed	5 / 124 (4.03%)	9 / 75 (12.00%)	
occurrences (all)	5	9	
Agitation			
subjects affected / exposed	7 / 124 (5.65%)	2 / 75 (2.67%)	
occurrences (all)	8	3	
Anxiety			
subjects affected / exposed	4 / 124 (3.23%)	3 / 75 (4.00%)	
occurrences (all)	6	3	
Insomnia			
subjects affected / exposed	5 / 124 (4.03%)	6 / 75 (8.00%)	
occurrences (all)	6	7	
Intentional self-injury			
subjects affected / exposed	4 / 124 (3.23%)	0 / 75 (0.00%)	
occurrences (all)	4	0	
Irritability			
subjects affected / exposed	9 / 124 (7.26%)	5 / 75 (6.67%)	
occurrences (all)	10	6	
Mental status changes			
subjects affected / exposed	3 / 124 (2.42%)	0 / 75 (0.00%)	
occurrences (all)	4	0	
Mood altered			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	2	

Panic attack			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences (all)	0	0	
Sleep disorder			
subjects affected / exposed	6 / 124 (4.84%)	4 / 75 (5.33%)	
occurrences (all)	6	4	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 124 (5.65%)	5 / 75 (6.67%)	
occurrences (all)	8	5	
Anticonvulsant drug level increased			
subjects affected / exposed	2 / 124 (1.61%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 124 (4.03%)	3 / 75 (4.00%)	
occurrences (all)	7	4	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Blood iron decreased			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Blood prolactin increased			
subjects affected / exposed	2 / 124 (1.61%)	3 / 75 (4.00%)	
occurrences (all)	2	4	
Blood triglycerides increased			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Blood urea increased			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Eosinophil count increased			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			

subjects affected / exposed	4 / 124 (3.23%)	9 / 75 (12.00%)	
occurrences (all)	4	9	
Hepatic enzyme increased			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
International normalised ratio increased			
subjects affected / exposed	1 / 124 (0.81%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Liver function test increased			
subjects affected / exposed	1 / 124 (0.81%)	5 / 75 (6.67%)	
occurrences (all)	1	10	
Platelet count decreased			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Prothrombin time prolonged			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	7 / 124 (5.65%)	9 / 75 (12.00%)	
occurrences (all)	7	9	
Weight increased			
subjects affected / exposed	3 / 124 (2.42%)	3 / 75 (4.00%)	
occurrences (all)	3	5	
White blood cell count decreased			
subjects affected / exposed	3 / 124 (2.42%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
White blood cell count increased			
subjects affected / exposed	3 / 124 (2.42%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	4 / 124 (3.23%)	0 / 75 (0.00%)	
occurrences (all)	4	0	
Arthropod bite			

subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Contusion			
subjects affected / exposed	6 / 124 (4.84%)	4 / 75 (5.33%)	
occurrences (all)	8	5	
Eye contusion			
subjects affected / exposed	2 / 124 (1.61%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Face injury			
subjects affected / exposed	2 / 124 (1.61%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Fall			
subjects affected / exposed	13 / 124 (10.48%)	8 / 75 (10.67%)	
occurrences (all)	23	9	
Foot fracture			
subjects affected / exposed	2 / 124 (1.61%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Head injury			
subjects affected / exposed	4 / 124 (3.23%)	0 / 75 (0.00%)	
occurrences (all)	5	0	
Laceration			
subjects affected / exposed	9 / 124 (7.26%)	4 / 75 (5.33%)	
occurrences (all)	13	4	
Ligament sprain			
subjects affected / exposed	1 / 124 (0.81%)	3 / 75 (4.00%)	
occurrences (all)	1	3	
Lip injury			
subjects affected / exposed	3 / 124 (2.42%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
Skin abrasion			
subjects affected / exposed	2 / 124 (1.61%)	3 / 75 (4.00%)	
occurrences (all)	2	3	
Tooth fracture			
subjects affected / exposed	5 / 124 (4.03%)	1 / 75 (1.33%)	
occurrences (all)	5	1	
Upper limb fracture			

subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Nervous system disorders			
Ataxia			
subjects affected / exposed	4 / 124 (3.23%)	4 / 75 (5.33%)	
occurrences (all)	5	7	
Balance disorder			
subjects affected / exposed	2 / 124 (1.61%)	2 / 75 (2.67%)	
occurrences (all)	3	2	
Dizziness			
subjects affected / exposed	4 / 124 (3.23%)	4 / 75 (5.33%)	
occurrences (all)	5	5	
Drooling			
subjects affected / exposed	3 / 124 (2.42%)	2 / 75 (2.67%)	
occurrences (all)	4	2	
Generalised tonic-clonic seizure			
subjects affected / exposed	4 / 124 (3.23%)	2 / 75 (2.67%)	
occurrences (all)	4	2	
Headache			
subjects affected / exposed	9 / 124 (7.26%)	5 / 75 (6.67%)	
occurrences (all)	22	10	
Hypersomnia			
subjects affected / exposed	0 / 124 (0.00%)	0 / 75 (0.00%)	
occurrences (all)	0	0	
Hypokinesia			
subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Lethargy			
subjects affected / exposed	3 / 124 (2.42%)	4 / 75 (5.33%)	
occurrences (all)	4	4	
Psychomotor hyperactivity			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Sedation			
subjects affected / exposed	2 / 124 (1.61%)	3 / 75 (4.00%)	
occurrences (all)	2	3	

Seizure			
subjects affected / exposed	32 / 124 (25.81%)	16 / 75 (21.33%)	
occurrences (all)	49	23	
Somnolence			
subjects affected / exposed	15 / 124 (12.10%)	24 / 75 (32.00%)	
occurrences (all)	21	29	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 124 (3.23%)	2 / 75 (2.67%)	
occurrences (all)	4	2	
Eosinophilia			
subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Increased tendency to bruise			
subjects affected / exposed	0 / 124 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 124 (1.61%)	2 / 75 (2.67%)	
occurrences (all)	3	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 124 (3.23%)	3 / 75 (4.00%)	
occurrences (all)	8	3	
Abdominal pain upper			
subjects affected / exposed	3 / 124 (2.42%)	2 / 75 (2.67%)	
occurrences (all)	4	2	
Constipation			
subjects affected / exposed	12 / 124 (9.68%)	9 / 75 (12.00%)	
occurrences (all)	16	18	
Diarrhoea			
subjects affected / exposed	50 / 124 (40.32%)	43 / 75 (57.33%)	
occurrences (all)	97	91	
Frequent bowel movements			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			

subjects affected / exposed	4 / 124 (3.23%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Mouth ulceration			
subjects affected / exposed	3 / 124 (2.42%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
Nausea			
subjects affected / exposed	3 / 124 (2.42%)	4 / 75 (5.33%)	
occurrences (all)	4	4	
Retching			
subjects affected / exposed	3 / 124 (2.42%)	3 / 75 (4.00%)	
occurrences (all)	4	3	
Salivary hypersecretion			
subjects affected / exposed	3 / 124 (2.42%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
Toothache			
subjects affected / exposed	4 / 124 (3.23%)	0 / 75 (0.00%)	
occurrences (all)	4	0	
Vomiting			
subjects affected / exposed	27 / 124 (21.77%)	13 / 75 (17.33%)	
occurrences (all)	45	22	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 124 (2.42%)	2 / 75 (2.67%)	
occurrences (all)	3	2	
Dermatitis diaper			
subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Erythema			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Pruritus			
subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	8 / 124 (6.45%)	4 / 75 (5.33%)	
occurrences (all)	8	4	

Rash maculo-papular			
subjects affected / exposed	0 / 124 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Urticaria			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	3	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	2 / 124 (1.61%)	3 / 75 (4.00%)	
occurrences (all)	2	3	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 124 (1.61%)	4 / 75 (5.33%)	
occurrences (all)	2	4	
Conjunctivitis			
subjects affected / exposed	8 / 124 (6.45%)	3 / 75 (4.00%)	
occurrences (all)	9	3	
Croup infectious			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Ear infection			
subjects affected / exposed	6 / 124 (4.84%)	3 / 75 (4.00%)	
occurrences (all)	10	5	
Gastroenteritis			
subjects affected / exposed	4 / 124 (3.23%)	2 / 75 (2.67%)	
occurrences (all)	9	3	
Gastroenteritis viral			
subjects affected / exposed	6 / 124 (4.84%)	3 / 75 (4.00%)	
occurrences (all)	8	3	
Influenza			
subjects affected / exposed	11 / 124 (8.87%)	4 / 75 (5.33%)	
occurrences (all)	11	5	

Nasopharyngitis			
subjects affected / exposed	19 / 124 (15.32%)	16 / 75 (21.33%)	
occurrences (all)	28	25	
Otitis media			
subjects affected / exposed	8 / 124 (6.45%)	4 / 75 (5.33%)	
occurrences (all)	11	4	
Pharyngitis			
subjects affected / exposed	8 / 124 (6.45%)	2 / 75 (2.67%)	
occurrences (all)	13	2	
Pharyngitis streptococcal			
subjects affected / exposed	12 / 124 (9.68%)	4 / 75 (5.33%)	
occurrences (all)	17	5	
Pneumonia			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Respiratory tract infection			
subjects affected / exposed	1 / 124 (0.81%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	4 / 124 (3.23%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Sinusitis			
subjects affected / exposed	7 / 124 (5.65%)	2 / 75 (2.67%)	
occurrences (all)	8	2	
Tonsillitis			
subjects affected / exposed	1 / 124 (0.81%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Upper respiratory tract infection			
subjects affected / exposed	22 / 124 (17.74%)	10 / 75 (13.33%)	
occurrences (all)	41	11	
Urinary tract infection			
subjects affected / exposed	7 / 124 (5.65%)	2 / 75 (2.67%)	
occurrences (all)	8	3	
Viral infection			
subjects affected / exposed	4 / 124 (3.23%)	5 / 75 (6.67%)	
occurrences (all)	10	7	

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 124 (3.23%) 5	3 / 75 (4.00%) 5	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	22 / 124 (17.74%) 26	23 / 75 (30.67%) 29	
Dehydration subjects affected / exposed occurrences (all)	3 / 124 (2.42%) 3	2 / 75 (2.67%) 2	
Diet refusal subjects affected / exposed occurrences (all)	0 / 124 (0.00%) 0	0 / 75 (0.00%) 0	
Increased appetite subjects affected / exposed occurrences (all)	3 / 124 (2.42%) 3	0 / 75 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2017	Incorporated additional updates to the trial design: • Statistical analysis was amended to reflect the re-categorization of secondary endpoints. • Clarification of exclusion criteria relating to mTOR inhibitors to reflect their changing regulatory approval status. • Provision was made to extend the OLE for subjects in the US and Poland. subjects in other countries would be able to access continued supply of investigational medicinal product (IMP) by alternative schemes. • Administration of cannabidiol through a gastrostomy (G)/nasogastric (NG) feeding tube was added as an option after consultation with the medical monitor. • Direction included that subject/caregiver to record information about meals on pharmacokinetic testing days.
07 August 2018	Incorporated additional updates to the trial design: • An inclusion criterion was added to ensure that eligible subjects must be taking 1 or more AEDs at a dose which had been stable for at least 4 weeks prior to screening. • Inclusion criteria amended to clarify that eligible subjects must have a well-documented clinical history of epilepsy which is not completely controlled by their current AEDs. • Clarification about the 4-hour post-dose 12-lead electrocardiogram (ECG). • Clarification on PK blood samples. • For consistency with the Schedule of Assessments, the protocol has been amended to clarify that eligibility must be assessed at Screening and Randomization according to the criteria. • Clarification that continued use of GWP42003-P following the 'End of Treatment' visit of the OLE refers to use of GWP42003-P outside of the GWEP1521 trial. • Clarification that in subjects with profound cognitive impairment aged 6 years or older, where completion of the Columbia-Suicide Severity Rating Scale (C-SSRS) is not appropriate, suicidality is assessed by the investigator's clinical judgment following interview of the subject. • Clarification that the Study Medication Use and Behavior Survey should be administered at the final dosing visit of the blinded phase and again at the final dosing visit of the OLE. • Clarification that the blinded phase of this study would be locked and unblinded prior to completion of the OLE and that the SAP covering the blinded phase would be finalized prior to unblinding the blinded phase.
06 September 2018	Incorporated updates to include: • Changes in primary endpoint analysis method and wording • Changes to the proposed sensitivity analyses
23 April 2019	Incorporated updates to change the order of the hierarchy of testing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported