



Clinical trial results:

A randomised, double blind, placebo controlled, parallel group, dose ranging study of GWP42004 as add on to metformin in the treatment of participants with Type 2 diabetes.

Summary

EudraCT number	2013-001140-61
Trial protocol	GB
Global end of trial date	29 December 2015

Results information

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

Trial information

Trial identification

Sponsor protocol code	GWDM1302
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02053272
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 December 2015
Global end of trial reached?	Yes
Global end of trial date	29 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of 2, 5 and 15 milligrams (mg) twice daily of GWP42004 compared with placebo by assessing the impact of treatment on glycaemic control in the treatment of participants with Type 2 diabetes.

Protection of trial subjects:

This trial was conducted in compliance with International Conference on Harmonisation Good Clinical Practice guidelines for conducting, recording, and reporting trials, as well as for archiving essential documents. Consistent with ethical principles for the protection of human research participants, no study procedures were performed on study participants until written consent had been obtained from them. The informed consent form, protocol, and amendments for this trial were submitted to and approved by the Institutional Review Board or Ethics Committee at each participating trial site.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Romania: 166
Country: Number of subjects enrolled	United Kingdom: 41
Worldwide total number of subjects	207
EEA total number of subjects	207

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	139

From 65 to 84 years	68
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult participants had been diagnosed with type 2 diabetes, received oral metformin (≥ 1000 mg/day) for ≥ 3 months prior to screening, maintained stable metformin dose for trial duration, had not taken insulin in the last year, had glycosylated haemoglobin A1c (HbA1c) levels $>7\%$ - $\leq 9\%$, and body mass index (BMI) >23 - <40 kilograms (kg)/metre (m)².

Period 1

Period 1 title	Baseline, Treatment, Follow-up (overall period)
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	GWP42004, 2 mg twice daily

Arm description:

Participants self-administered oral, active investigational medicinal product (IMP) GWP42004, 2 mg in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.

Arm type	Experimental
Investigational medicinal product name	GWP42004
Investigational medicinal product code	
Other name	$\Delta 9$ -tetrahydrocannabivarin
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GWP42004 was presented as a hard gelatin capsule containing 2 mg GWP42004 ($\Delta 9$ -tetrahydrocannabivarin) and excipients macrogolglycerol ricinoleate and oleoyl macrogol-6-glycerides. The capsule shells contained indigo carmine - Federal Food, Drug, and Cosmetic (FD&C) blue number 2, titanium dioxide (E171), and yellow iron oxide colourings.

Arm title	GWP42004, 5 mg twice daily
------------------	----------------------------

Arm description:

Participants self-administered oral, active IMP GWP42004, 5 mg in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.

Arm type	Experimental
Investigational medicinal product name	GWP42004
Investigational medicinal product code	
Other name	$\Delta 9$ -tetrahydrocannabivarin
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GWP42004 was presented as a hard gelatin capsule containing 5 mg GWP42004 ($\Delta 9$ -tetrahydrocannabivarin) and excipients macrogolglycerol ricinoleate and oleoyl macrogol-6-glycerides. The capsule shells contained indigo carmine - FD&C blue number 2, titanium dioxide (E171), and yellow iron oxide colourings.

Arm title	GWP42004, 15 mg twice daily
Arm description:	
Participants self-administered oral, active IMP GWP42004, 15 mg in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.	
Arm type	Experimental
Investigational medicinal product name	GWP42004
Investigational medicinal product code	
Other name	Δ9-tetrahydrocannabivarin
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GWP42004 was presented as a hard gelatin capsule containing 15 mg GWP42004 (Δ9-tetrahydrocannabivarin) and excipients macrogolglycerol ricinoleate and oleoyl macrogol-6-glycerides. The capsule shells contained indigo carmine - FD&C blue number 2, titanium dioxide (E171), and yellow iron oxide colourings.

Arm title	Placebo, twice daily
------------------	----------------------

Arm description:

Participants self-administered oral placebo in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical to GWP42004 treatment arms.

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

Dosage and administration details:

Placebo was presented as a hard gelatin capsule containing excipients macrogolglycerol ricinoleate and oleoyl macrogol-6-glycerides. The capsule shells contained indigo carmine - FD&C blue number 2, titanium dioxide (E171), and yellow iron oxide colourings.

Number of subjects in period 1	GWP42004, 2 mg twice daily	GWP42004, 5 mg twice daily	GWP42004, 15 mg twice daily
Started	54	53	52
Received at Least 1 Dose of Study Drug	54	53	52
Safety Population	54	53	52
Intent to Treat (ITT) Population	52	53	52
Completed	48	50	48
Not completed	6	3	4
Withdrawn by investigator	1	-	1
Consent withdrawn by subject	1	2	-
Adverse event, non-fatal	2	-	3
Lost to follow-up	1	-	-
Met protocol specified withdrawal criteria	1	1	-

Number of subjects in period 1	Placebo, twice daily
Started	48
Received at Least 1 Dose of Study Drug	48
Safety Population	48
Intent to Treat (ITT) Population	48
Completed	47
Not completed	1
Withdrawn by investigator	-
Consent withdrawn by subject	1
Adverse event, non-fatal	-
Lost to follow-up	-
Met protocol specified withdrawal criteria	-

Baseline characteristics

Reporting groups

Reporting group title	GWP42004, 2 mg twice daily
Reporting group description:	
Participants self-administered oral, active investigational medicinal product (IMP) GWP42004, 2 mg in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.	
Reporting group title	GWP42004, 5 mg twice daily
Reporting group description:	
Participants self-administered oral, active IMP GWP42004, 5 mg in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.	
Reporting group title	GWP42004, 15 mg twice daily
Reporting group description:	
Participants self-administered oral, active IMP GWP42004, 15 mg in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.	
Reporting group title	Placebo, twice daily
Reporting group description:	
Participants self-administered oral placebo in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical to GWP42004 treatment arms.	

Reporting group values	GWP42004, 2 mg twice daily	GWP42004, 5 mg twice daily	GWP42004, 15 mg twice daily
Number of subjects	54	53	52
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	36	31	39
From 65-84 years	18	22	13
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	60.4	61.4	59.2
standard deviation	± 8.83	± 8.96	± 9.59
Gender categorical			
Units: Subjects			
Female	25	23	24
Male	29	30	28

Reporting group values	Placebo, twice daily	Total	
Number of subjects	48	207	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	33	139	
From 65-84 years	15	68	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	59.5		
standard deviation	± 8.81	-	
Gender categorical Units: Subjects			
Female	25	97	
Male	23	110	

End points

End points reporting groups

Reporting group title	GWP42004, 2 mg twice daily
-----------------------	----------------------------

Reporting group description:

Participants self-administered oral, active investigational medicinal product (IMP) GWP42004, 2 mg in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.

Reporting group title	GWP42004, 5 mg twice daily
-----------------------	----------------------------

Reporting group description:

Participants self-administered oral, active IMP GWP42004, 5 mg in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.

Reporting group title	GWP42004, 15 mg twice daily
-----------------------	-----------------------------

Reporting group description:

Participants self-administered oral, active IMP GWP42004, 15 mg in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.

Reporting group title	Placebo, twice daily
-----------------------	----------------------

Reporting group description:

Participants self-administered oral placebo in the fasted state, 1 capsule, twice daily, for 12 weeks, approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical to GWP42004 treatment arms.

Subject analysis set title	ITT Analysis Set
----------------------------	------------------

Subject analysis set type	Intention-to-treat
---------------------------	--------------------

Subject analysis set description:

The ITT analysis set included all randomized participants who took at least 1 dose of IMP and had post-baseline efficacy data.

Primary: Change From Baseline To The End Of Treatment In Mean Glycosylated Haemoglobin A1c (HbA1c) Level

End point title	Change From Baseline To The End Of Treatment In Mean Glycosylated Haemoglobin A1c (HbA1c) Level
-----------------	---

End point description:

The change from baseline to the end of the 12-week treatment in mean HbA1c levels was analysed for participants with type 2 diabetes following 12 weeks of IMP (GWP42004 or placebo) treatment (or until withdrawal), as an add on to metformin.

Analysis of covariance (ANCOVA) was used, with dose included as a categorical variable. Baseline HbA1c was included as a covariate; dose, sex, and centre group were included as factors. Last visit using last observation carried forward (LOCF) was used where appropriate. If a participant in the ITT analysis set had no post-baseline HbA1c levels, baseline observation carried forward (BOCF) was used.

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

End point timeframe:

Baseline, End of Treatment

End point values	GWP42004, 2 mg twice daily	GWP42004, 5 mg twice daily	GWP42004, 15 mg twice daily	Placebo, twice daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	53	52	48
Units: percent				
least squares mean (standard error)	-0.17 ($\pm$ 0.11)	-0.16 ($\pm$ 0.11)	-0.22 ($\pm$ 0.11)	-0.16 ($\pm$ 0.11)

Statistical analyses

Statistical analysis title	GWP42004, 2 mg twice daily versus Placebo
Comparison groups	GWP42004, 2 mg twice daily v Placebo, twice daily
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.96
Method	ANCOVA
Parameter estimate	Least square mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	GWP42004, 5 mg twice daily versus Placebo
Comparison groups	GWP42004, 5 mg twice daily v Placebo, twice daily
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.983
Method	ANCOVA
Parameter estimate	Least square mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	GWP42004, 15 mg twice daily versus Placebo
-----------------------------------	--

Comparison groups	Placebo, twice daily v GWP42004, 15 mg twice daily
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.677
Method	ANCOVA
Parameter estimate	Least square mean difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.22
Variability estimate	Standard error of the mean
Dispersion value	0.14

Secondary: Change From Baseline To The End Of Treatment In Mean Fasting Plasma Glucose Level

End point title	Change From Baseline To The End Of Treatment In Mean Fasting Plasma Glucose Level
-----------------	---

End point description:

The change from baseline to the end of the 12-week treatment in mean fasting plasma glucose levels was analysed for participants with type 2 diabetes following 12 weeks of IMP (GWP42004 or placebo) treatment (or until withdrawal), as an add on to metformin.

Analysis of covariance (ANCOVA) was used, with dose included as a categorical variable. Baseline fasting plasma glucose level was included as a covariate; dose, sex, and centre group were included as factors. Last visit using LOCF was used where appropriate.

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

End point timeframe:

Baseline, End of Treatment

End point values	GWP42004, 2 mg twice daily	GWP42004, 5 mg twice daily	GWP42004, 15 mg twice daily	Placebo, twice daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	53	52	48
Units: millimole/litre				
least squares mean (standard error)	-0.18 (± 0.27)	-0.02 (± 0.28)	-0.49 (± 0.26)	-0.55 (± 0.28)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The End Of Treatment In Mean Serum Fructosamine Levels

End point title	Change From Baseline To The End Of Treatment In Mean
-----------------	--

End point description:

The change from baseline to the end of the 12-week treatment in mean serum fructosamine levels was analysed for participants with type 2 diabetes following 12 weeks of IMP (GWP42004 or placebo) treatment (or until withdrawal), as an add on to metformin.

Analysis of covariance (ANCOVA) was used, with dose included as a categorical variable. Baseline serum fructosamine level was included as a covariate; dose, sex, and centre group were included as factors. Last visit using LOCF was used where appropriate.

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

End point timeframe:

Baseline, End of Treatment

End point values	GWP42004, 2 mg twice daily	GWP42004, 5 mg twice daily	GWP42004, 15 mg twice daily	Placebo, twice daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	53	52	48
Units: micromole(s)/litre				
least squares mean (standard error)	-14.90 ($\pm$ 5.23)	-8.59 ($\pm$ 5.24)	-9.65 ($\pm$ 5.05)	-7.51 ($\pm$ 5.31)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline To The End Of Treatment In Mean Serum Glucose Levels In The Oral Glucose Tolerance Test [OGTT])

End point title	Change From Baseline To The End Of Treatment In Mean Serum Glucose Levels In The Oral Glucose Tolerance Test [OGTT])
-----------------	--

End point description:

The change from baseline to the end of the 12-week treatment in mean plasma glucose levels 30 minutes and 2 hours post glucose challenge using the OGTT was analysed for participants with type 2 diabetes following 12 weeks of IMP (GWP42004 or placebo) treatment (or until withdrawal), as an add on to metformin.

Analysis of covariance (ANCOVA) was used, with dose included as a categorical variable. The baseline value of the respective OGTT parameter was included as a covariate; dose, sex, and centre group were included as factors. Last visit using LOCF was used where appropriate.

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

End point timeframe:

Baseline, End of Treatment

End point values	GWP42004, 2 mg twice daily	GWP42004, 5 mg twice daily	GWP42004, 15 mg twice daily	Placebo, twice daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	53	52	48
Units: millimole(s)/litre				
least squares mean (standard error)				
Glucose Levels After 30 Minutes	0.84 (± 0.30)	-0.26 (± 0.29)	-0.04 (± 0.29)	0.49 (± 0.31)
Glucose Levels After 120 Minutes	0.20 (± 0.42)	0.11 (± 0.43)	-0.01 (± 0.42)	0.84 (± 0.46)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening (Visit 1, Day -7) up to the safety follow-up (Day 92)

Adverse event reporting additional description:

An adverse event (AE) was any new, unintended symptom, diagnosis, or worsening of pre-existing condition presenting between screening and the safety follow-up call that may or may not be related to IMP, or any event that resulted from a trial procedure. Safety analysis set included randomized participants who received at least 1 dose of IMP.

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

Dictionary used

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

Dictionary version	16.1
--------------------	------

Reporting groups

Reporting group title	GWP42004, 2 mg twice daily
-----------------------	----------------------------

Reporting group description:

Participants self-administered oral, active investigational medicinal product (IMP) GWP42004, 2 mg in the fasted state, twice daily approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.

Reporting group title	GWP42004, 5 mg twice daily
-----------------------	----------------------------

Reporting group description:

Participants self-administered oral, active IMP GWP42004, 5 mg in the fasted state, twice daily approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.

Reporting group title	GWP42004, 15 mg twice daily
-----------------------	-----------------------------

Reporting group description:

Participants self-administered oral, active IMP GWP42004, 15 mg in the fasted state, twice daily approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.

Reporting group title	Placebo, twice daily
-----------------------	----------------------

Reporting group description:

Participants self-administered oral IMP placebo in the fasted state, twice daily approximately 30 minutes before breakfast and approximately 30 minutes before the evening meal, typically 12 hours apart. The total dose administered within any 24 hour interval was 2 capsules and the number of capsules administered was identical in all arms and at all dose levels.

Serious adverse events	GWP42004, 2 mg twice daily	GWP42004, 5 mg twice daily	GWP42004, 15 mg twice daily
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	1 / 52 (1.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 54 (0.00%)	0 / 53 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	0 / 52 (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
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	0 / 53 (0.00%)	0 / 52 (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

Serious adverse events	Placebo, twice daily		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 48 (2.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophageal ulcer haemorrhage			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	GWP42004, 2 mg twice daily	GWP42004, 5 mg twice daily	GWP42004, 15 mg twice daily
Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 54 (9.26%)	4 / 53 (7.55%)	2 / 52 (3.85%)
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 3	2 / 53 (3.77%) 3	1 / 52 (1.92%) 1
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 54 (1.85%) 1	2 / 53 (3.77%) 2	1 / 52 (1.92%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 54 (1.85%) 1	2 / 53 (3.77%) 2	0 / 52 (0.00%) 0

Non-serious adverse events	Placebo, twice daily		
Total subjects affected by non-serious adverse events subjects affected / exposed	9 / 48 (18.75%)		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 48 (8.33%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 48 (8.33%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported