Clinical trial results:
Multicenter, randomized, double-blind, two-period, placebo controlled, forced-titration proof of concept crossover study to compare QGC001 with placebo in patients with grade I or II essential hypertension

Summary

EudraCT number	2014-003071-37
Trial protocol	FR
Global end of trial date	13 April 2016

Results information

Result version number	v1 (current)
This version publication date	18 May 2017
First version publication date	18 May 2017
Summary attachment (see zip file)	synopsisQGC001 (synopsisQGC001.pdf)

Trial information

Trial identification

Sponsor protocol code	QGC001/2QG1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Quantum Genomics
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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	13 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 April 2016
Global end of trial reached?	Yes
Global end of trial date	13 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the BP lowering effect of 4-week administration of QGC001 oral doses in patients with grade I or II essential hypertension compared to placebo.

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, ethical principles stated in the Declaration of Helsinki and applicable regulatory requirements. After the subject has ended his/her participation in the trial, the investigator provided appropriate medication and/or arranged access to appropriate care for the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 February 2015
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	France: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	31

From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was performed in male and female of non-childbearing potential, aged 18 to 75 years, with a BMI of 18 to 40 kg/m2, with essential grade I or II hypertension, a diagnosis of permanent hypertension, an estimated glomerular filtration rate ≥ 60 mL/min/1.73 m2, and a signed and dated informed consent form before any screening procedure.

Pre-assignment

Screening details:

50 subjects were screened and 40 were included in the run-in period (= pre-assignment period). The screening period included a period of tapering and discontinuation of current antihypertensive therapy for 2 weeks if needed. Patients untreated at screening directly entered the run-in period, which consisted of 2 weeks of placebo treatment.

Pre-assignment period milestones

Number of subjects started	40
Number of subjects completed	34[1]

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 5
Reason: Number of subjects	Consent withdrawn by subject: 1

Notes:

[1] - The number of subjects reported to be in the pre-assignment period is not consistent with the number starting period 1. It is expected that the number completing the pre-assignment period are also present in the arms in period 1.
Justification: During the pre-assignement period, 6 subjects were withdrawn.

Period 1

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

Blinding implementation details:

The randomization was stratified by center, and investigating centers allocated the therapeutic units (TU) by order of patient’s inclusion in each center, using the TU kits available to each center.

Arms

Are arms mutually exclusive?	No
Arm title	QGC001

Arm description:

Patients were randomised to one of the 2 sequences of treatment, either QGC001/placebo or placebo/QGC001 (2-way cross over). Patients underwent two four-week treatment arms where they received either QGC001 or placebo. Each arm was separated by a two-week washout period where patient received placebo (as one capsule every 12 hours (08:00 am and 20:00 pm) for one week followed by 2 capsules every 12 hours (08:00 am and 20:00h) for 1 week). This arm concerns the QGC001 treatment.

Arm type	Experimental
Investigational medicinal product name	QGC001 250 mg
Investigational medicinal product code	QGC001
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

In this arm, patients received QGC001 250 mg b.i.d. during one week, as one 250 mg capsule every 12 hours (08:00 am and 08:00 pm) followed by QGC001 500 mg b.i.d. during three weeks, as two 250 mg capsules every 12 hours (08:00 am and 08:00h).

Arm title	placebo

Arm description:

Patients were randomised to one of the 2 sequences of treatment, either QGC001/placebo or placebo/QGC001 (2-way cross over). Patients underwent two four-week treatment arms where they received either QGC001 or placebo. Each arm was separated by a two-week washout period where patient received placebo (as one capsule every 12 hours (08:00 am and 20:00 pm) for one week followed by 2 capsules every 12 hours (08:00 am and 20:00h) for 1 week). This arm concerns the placebo treatment.

Arm type	Placebo
Investigational medicinal product name	QGC001 placebo
Investigational medicinal product code	QGC001
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

In this arm, patients received placebo during one week, as one capsule every 12 hours (08:00 am and 08:00 pm) followed by placebo during three weeks, as 2 capsules every 12 hours (08:00 am and 08:00 pm).

Number of subjects in period 1	QGC001	placebo
Started	33	33
Completed	30	32
Not completed	3	1
Consent withdrawn by subject	1	-
Physician decision	-	1
Adverse event, non-fatal	2	-

Baseline characteristics

Reporting groups[1]	
Reporting group title	cross-over period
Reporting group description: -	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: The worldwide number of subjects corresponds to the number of subjects who started the pre-assignment period, whereas the number of subjects in the baseline period corresponds to the number of subjects who entered the cross-over period after the pre-assignement period. During the pre-assignement period, 6 subjects were withdrawn.

Reporting group values	cross-over period	Total	
Number of subjects	34	34	
Age categorical Units: Subjects			
Adults (18-64 years)	27	27	
From 65-84 years	7	7	
Age continuous Units: years			
arithmetic mean	56.6		
standard deviation	± 9.1	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	25	25	

End points

End points reporting groups

Reporting group title	QGC001

Reporting group description:

Patients were randomised to one of the 2 sequences of treatment, either QGC001/placebo or placebo/QGC001 (2-way cross over). Patients underwent two four-week treatment arms where they received either QGC001 or placebo. Each arm was separated by a two-week washout period where patient received placebo (as one capsule every 12 hours (08:00 am and 20:00 pm) for one week followed by 2 capsules every 12 hours (08:00 am and 20:00h) for 1 week). This arm concerns the QGC001 treatment.

Reporting group title	placebo

Reporting group description:

Patients were randomised to one of the 2 sequences of treatment, either QGC001/placebo or placebo/QGC001 (2-way cross over). Patients underwent two four-week treatment arms where they received either QGC001 or placebo. Each arm was separated by a two-week washout period where patient received placebo (as one capsule every 12 hours (08:00 am and 20:00 pm) for one week followed by 2 capsules every 12 hours (08:00 am and 20:00h) for 1 week). This arm concerns the placebo treatment.

Primary: day-time mean SBP changes from baseline

End point title	day-time mean SBP changes from baseline

End point description:

End point type	Primary

End point timeframe:

the primary endpoint was the comparison of change from baseline of daytime mean SBP as calculated from the individual ABPM after 4 weeks of treatment between treatments, in the ITT set.

End point values	QGC001	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: mmHg				
arithmetic mean (standard deviation)	-1.88 (± 8.13)	0.68 (± 9.34)		

Statistical analyses

Statistical analysis title	day-time mean SBP changes ANOVA

Statistical analysis description:

The comparisons between treatments of daytime mean SBP were analyzed using an analysis of variance (ANOVA) on change from baseline to 4 weeks of treatment with treatment group, sequence, period and center as fixed effects and subject within sequence as random effect. The estimate and the 95% CI of the difference between QGC001 and placebo were calculated.

Comparison groups	QGC001 v placebo

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1573
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.47
upper limit	1.1

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Subjects were required to report any AE that occurred after informed consent was signed. All AEs that occurred from the time of informed consent until 1 week after 24 hours after Day 8 of the second arm of the sequence of treatment were recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	QGC001

Reporting group description:

Patients underwent a run-in epriod of 2 weeks during which they recieved placebo, followed by two four-week treatment arms, in which they received either QGC001 or placebo (2-way cross-over), separated by a two-week washout period where they received placebo (as one capsule every 12 hours (08:00 am and 20:00 pm) for one week followed by 2 capsules every 12 hours (08:00 am and 20:00h) for 1 week. This reporting group concerns the QGC001 treatment.

Reporting group title	placebo

Reporting group description:

Patients underwent two four-week treatment periods separated by a two-week washout period where they received placebo (as one capsule every 12 hours (08:00 am and 20:00 pm) for one week followed by 2 capsules every 12 hours (08:00 am and 20:00h) for 1 week. In each period, they received either QGC001 or placebo. This arm concerns the placebo treatment.

Reporting group title	Run-in Period

Reporting group description: -

Reporting group title	washout period

Reporting group description: -

Serious adverse events	QGC001	placebo	Run-in Period
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	0 / 33 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 33 (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
Skin and subcutaneous tissue disorders			
Rash macular			

subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 33 (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

Serious adverse events	washout period		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	QGC001	placebo	Run-in Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	2 / 33 (6.06%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	2 / 33 (6.06%)
occurrences (all)	1	1	2

Non-serious adverse events	washout period		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 32 (6.25%)		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2015	The purpose of the amendment was to modify inclusion criterion N°5, in order to reflect international guidelines and the upper limits of normal range for the definition of the mean SBP and DBP for the diagnosis of permanent hypertension. In V1.0 of the protocol, inclusion criterion N°5 was: 5/ Diagnosis of permanent hypertension confirmed by a mean SBP or DBP higher than 135 or 85 mmHg on daytime ambulatory blood pressure monitoring (ABPM) after a 2week placebo run-in period. In V2.0 of the protocol, the criterion became:5/ Diagnosis of permanent hypertension confirmed by a mean SBP or DBP equal to or higher than 135 or 85 mmHg on daytime ambulatory blood pressure monitoring (ABPM) after a 2-week placebo run-in period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported