

**Clinical trial results:****A Phase 3, Double-blind, Placebo-controlled, Efficacy and Safety Study of Firibastat (QGC001) Administered Orally, Twice Daily, Over 12 Weeks in Difficult-to-treat/Resistant Hypertensive Subjects****Summary**

EudraCT number	2019-004509-29
Trial protocol	FR DE PL ES CZ HU BG
Global end of trial date	20 September 2022

Results information

Result version number	v1 (current)
This version publication date	04 March 2023
First version publication date	04 March 2023
Summary attachment (see zip file)	CSR Synopsis (FRESH_CSR_VF_Summary_20Jan2023.pdf)

Trial information**Trial identification**

Sponsor protocol code	QGC001-3QG1
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04277884
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Quantum Genomics
Sponsor organisation address	33 rue Marbeuf, Paris, France,
Public contact	Bruno Besse, Quantum Genomics, 33 185347770, bruno.besse@quantum-genomics.com
Scientific contact	Bruno Besse, Quantum Genomics, 33 185347770, bruno.besse@quantum-genomics.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	07 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 September 2022
Global end of trial reached?	Yes
Global end of trial date	20 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the effects of administration of fribastat (QGC001) 500 mg oral (po) twice daily (bis in die [bid]) on blood pressure (BP) over 12 weeks in subjects with uncontrolled primary HTN despite being treated with 2 classes of antihypertensive therapies, at the maximum tolerated doses (MTDs). The secondary objective is to assess the safety of fribastat (QGC001).

Protection of trial subjects:

Subjects were followed for a period of 3 months after randomization with regular visits (every month) and criteria of discontinuation were added in the protocol on some safety criteria.

A 28 days FU visit after last IP intake was planned.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 May 2020
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	Poland: 129
Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	Bulgaria: 45
Country: Number of subjects enrolled	Czechia: 28
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Brazil: 54
Country: Number of subjects enrolled	Canada: 44
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	United States: 124
Worldwide total number of subjects	514
EEA total number of subjects	287

Notes:

Subjects enrolled per age group

In utero	0
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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)	253
From 65 to 84 years	256
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

Target population: Subjects with uncontrolled primary HTN despite being treated with at least 3 classes of antihypertensive therapies, including a diuretic, for treatment-resistant subjects or 2 classes of antihypertensive therapies (including or not including a diuretic), for difficult-to-treat subjects at the MTDs.

Pre-assignment

Screening details:

Screening visit is followed by a Run-in period of 28 days. During Run-in the subject is requested to take his/her current HTN treatment everyday.

A measure of APBM is done at the end of the Run-In period and the subject is eligible with an ABPM measurement with a mean systolic daytime ABP >135 mmHg after the Run-in Period.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
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Arm title	Firibastat 500mg BID
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Arm description: -

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

Dosage and administration details:

Dose: 500 mg (2×250 mg capsules) bid

Arm title	Placebo
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Arm description: -

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

Dosage and administration details:

Dose: 2 capsules bid

Number of subjects in period 1	Firibastat 500mg BID	Placebo
Started	255	259
Completed	204	219
Not completed	51	40
Adverse event, serious fatal	1	-
Physician decision	1	2
Consent withdrawn by subject	11	8
Adverse event, non-fatal	14	9
Various other reasons	9	17
Skin reaction	13	1
Severe hypertension	-	1
Lost to follow-up	1	1
Protocol deviation	1	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment period
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Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	514	514	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	63.4		
full range (min-max)	27 to 88	-	
Gender categorical Units: Subjects			
Female	214	214	
Male	300	300	

End points

End points reporting groups

Reporting group title	Firibastat 500mg BID
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description: All randomized subjects with at least one consumption of study product (Firibastat or placebo).	
Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description: All Full analysis set subjects without any major for primary endpoint deviation to the present protocol.	

Primary: Change in systolic AOPB from baseline to week 12

End point title	Change in systolic AOPB from baseline to week 12
End point description:	
End point type	Primary
End point timeframe: Week 12	

End point values	Firibastat 500mg BID	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	259		
Units: mmHg				
arithmetic mean (confidence interval 95%)	-7.82 (-9.79 to -5.85)	-7.85 (-9.77 to -5.93)		

Statistical analyses

Statistical analysis title	Primary analysis of the primary efficacy endpoint
Statistical analysis description: The main criterion will be analyzed with a mixed model with repeated measures (MMRM) with baseline as covariate and time, treatment and interaction between time and treatment as fixed effect as defined in part 2.5. Structure of the covariance matrix will be the unstructured one. Adjusted means (LS-Means) and difference of adjusted means between Firibastat and Placebo will be estimated with 95% confidence interval.	
Comparison groups	Firibastat 500mg BID v Placebo

Number of subjects included in analysis	514
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9844
Method	Mixed models analysis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From ICF signature at screening visit to end of study FU visit (28 days after and of treatment)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23
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Reporting groups

Reporting group title	Firibastat 500mg
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Firibastat 500mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 255 (2.75%)	3 / 259 (1.16%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps) MENINGIOMA			
subjects affected / exposed	1 / 255 (0.39%)	0 / 259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders CARDIAC FAILURE ACUTE			
subjects affected / exposed	1 / 255 (0.39%)	0 / 259 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 255 (0.00%)	1 / 259 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures PROSTATECTOMY			

subjects affected / exposed	0 / 255 (0.00%)	1 / 259 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 255 (0.00%)	1 / 259 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
NORMOCYTIC ANAEMIA			
subjects affected / exposed	1 / 255 (0.39%)	0 / 259 (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			
ASTHENIA			
subjects affected / exposed	1 / 255 (0.39%)	0 / 259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
RETINOPATHY HYPERTENSIVE			
subjects affected / exposed	0 / 255 (0.00%)	1 / 259 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 255 (0.39%)	0 / 259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MESENTERIC ARTERY STENOSIS			
subjects affected / exposed	1 / 255 (0.39%)	0 / 259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
DEPRESSION			

subjects affected / exposed	0 / 255 (0.00%)	1 / 259 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 PNEUMONIA			
subjects affected / exposed	1 / 255 (0.39%)	0 / 259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
MALNUTRITION			
subjects affected / exposed	1 / 255 (0.39%)	0 / 259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Firibastat 500mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 255 (39.22%)	88 / 259 (33.98%)	
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	4 / 255 (1.57%)	3 / 259 (1.16%)	
occurrences (all)	4	3	
Vascular disorders			
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	15 / 255 (5.88%)	16 / 259 (6.18%)	
occurrences (all)	18	18	
HYPERTENSION			
subjects affected / exposed	4 / 255 (1.57%)	3 / 259 (1.16%)	
occurrences (all)	4	3	
Cardiac disorders			
ATRIAL FIBRILATION			
subjects affected / exposed	2 / 255 (0.78%)	3 / 259 (1.16%)	
occurrences (all)	2	3	
Nervous system disorders			

HEADACHE subjects affected / exposed occurrences (all)	9 / 255 (3.53%) 9	9 / 259 (3.47%) 9	
DIZZINESS subjects affected / exposed occurrences (all)	7 / 255 (2.75%) 8	5 / 259 (1.93%) 6	
General disorders and administration site conditions			
FATIGUE subjects affected / exposed occurrences (all)	5 / 255 (1.96%) 5	3 / 259 (1.16%) 3	
ASTHENIA subjects affected / exposed occurrences (all)	4 / 255 (1.57%) 4	2 / 259 (0.77%) 2	
Gastrointestinal disorders			
DYSPEPSIA subjects affected / exposed occurrences (all)	1 / 255 (0.39%) 1	6 / 259 (2.32%) 6	
DIARRHOEA subjects affected / exposed occurrences (all)	3 / 255 (1.18%) 3	3 / 259 (1.16%) 3	
NAUSEA subjects affected / exposed occurrences (all)	3 / 255 (1.18%) 3	2 / 259 (0.77%) 2	
Skin and subcutaneous tissue disorders			
RASH subjects affected / exposed occurrences (all)	6 / 255 (2.35%) 6	2 / 259 (0.77%) 2	
PRURITUS subjects affected / exposed occurrences (all)	4 / 255 (1.57%) 4	2 / 259 (0.77%) 2	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA subjects affected / exposed occurrences (all)	5 / 255 (1.96%) 5	1 / 259 (0.39%) 1	
BACK PAIN			

subjects affected / exposed occurrences (all)	4 / 255 (1.57%) 4	2 / 259 (0.77%) 2	
Infections and infestations			
COVID-19			
subjects affected / exposed occurrences (all)	6 / 255 (2.35%) 6	8 / 259 (3.09%) 8	
NASOPHARYNGITIS			
subjects affected / exposed occurrences (all)	4 / 255 (1.57%) 4	2 / 259 (0.77%) 2	
INFLUENZA			
subjects affected / exposed occurrences (all)	2 / 255 (0.78%) 2	4 / 259 (1.54%) 4	
Metabolism and nutrition disorders			
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed occurrences (all)	6 / 255 (2.35%) 6	4 / 259 (1.54%) 4	
HYPERCHOLESTEROLEMIA			
subjects affected / exposed occurrences (all)	4 / 255 (1.57%) 4	4 / 259 (1.54%) 4	
HYPERURICAEMIA			
subjects affected / exposed occurrences (all)	3 / 255 (1.18%) 3	4 / 259 (1.54%) 5	
HYPERGLYCAEMIA			
subjects affected / exposed occurrences (all)	5 / 255 (1.96%) 5	1 / 259 (0.39%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 January 2020	Major changes : Added 'Subjects with moderate to severe hepatic impairment (Child-Pugh B or C)' to exclusion criteria #15. Added blood sample for coagulation test (prothrombin time) at Screening to enable assessment of Child-Pugh classification of hepatic impairment. Deleted analysis of blood samples for the biomarkers TNFR1 and copeptin.
27 October 2020	Harmonisation of all local Protocols Inclusion of COVID risk measures
31 March 2021	Eligible systolic automated office blood pressure (AOBP) range updated from 140-170 mmHg to 140-180 mmHg. Updated screen failures, to allow for rescreening

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported