Clinical trial results:
A Phase 2/3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Effect of GS-6615 on Exercise Capacity in Subjects with Symptomatic Hypertrophic Cardiomyopathy

Summary

EudraCT number	2013-004429-97
Trial protocol	GB NL IT
Global end of trial date	17 February 2017

Results information

Result version number	v1
This version publication date	30 December 2017
First version publication date	30 December 2017

Trial information

Trial identification

Sponsor protocol code	GS-US-361-1157

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02291237
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Clinical Trials Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trials Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.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	17 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 January 2017
Global end of trial reached?	Yes
Global end of trial date	17 February 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of eleclazine (GS-6615) on exercise capacity as measured by Peak oxygen uptake (VO2) achieved during cardiopulmonary exercise testing (CPET), in participants with symptomatic hypertrophic cardiomyopathy (HCM).

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 25
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	United States: 109
Worldwide total number of subjects	172
EEA total number of subjects	47

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)	169
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Asia, Australia, Europe and North America. The first participant was screened on 05 February 2015. The last study visit occurred on 22 February 2017.

Pre-assignment

Screening details:

264 participants were screened.

Period 1

Period 1 title	Overall Study (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	Eleclazine 30/3/6 mg

Arm description:

Single loading dose of eleclazine 30 mg (5 x 6 mg tablets) on Day 1, followed by 3 mg (1 x 3 mg tablet) daily maintenance dose until Week 12, then 6 mg (2 x 3 mg tablets) daily maintenance dose from Week 12 to at least Week 24

Arm type	Experimental
Investigational medicinal product name	Eleclazine 3 mg
Investigational medicinal product code	
Other name	GS-6615
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eleclazine 3 mg tablet (s) administered orally for at least 24 weeks

Investigational medicinal product name	Eleclazine 6 mg
Investigational medicinal product code	
Other name	GS-6615
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eleclazine 6 mg tablet (s) administered orally on Day 1

Arm title	Placebo

Arm description:

Placebo tablet (s) administered orally for at least 24 weeks

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

Dosage and administration details:

Placebo to match eleclazine for at least 24 weeks

Number of subjects in period 1	Eleclazine 30/3/6 mg	Placebo
Started	86	86
Completed	0	0
Not completed	86	86
Withdrew Consent	11	11
Adverse Event	1	3
Investigator's Discretion	-	3
Study Terminated by Sponsor	72	67
Lost to follow-up	-	2
Subject Required Prohibited Medication	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Eleclazine 30/3/6 mg
Reporting group description:	
Single loading dose of eleclazine 30 mg (5 x 6 mg tablets) on Day 1, followed by 3 mg (1 x 3 mg tablet) daily maintenance dose until Week 12, then 6 mg (2 x 3 mg tablets) daily maintenance dose from Week 12 to at least Week 24	
Reporting group title	Placebo
Reporting group description:	
Placebo tablet (s) administered orally for at least 24 weeks	

Reporting group values	Eleclazine 30/3/6 mg	Placebo	Total
Number of subjects	86	86	172
Age categorical Units: Subjects			
Age continuous			
Safety Analysis Set: all randomized participants who received at least 1 dose of study drug.			
Units: years			
arithmetic mean	46	48	
standard deviation	± 11.7	± 10.3	-
Gender categorical Units: Subjects			
Female	37	36	73
Male	49	50	99
Race Units: Subjects			
White	74	73	147
Black or African American	7	3	10
Asian	2	7	9
Other	2	1	3
Not Permitted	0	2	2
American Indian or Alaska Native	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	11	9	20
Not Hispanic or Latino	75	75	150
Not Permitted	0	2	2
Peak Oxygen Intake (VO2)			
Only 85 participants in the placebo arm with available data were analyzed.			
Units: mL/kg/min			
arithmetic mean	19.06	19.88	
standard deviation	± 4.853	± 4.645	-
Minnesota Living With Heart Failure Questionnaire (MLHFQ) Units: Score			
arithmetic mean	40.22	38.80	

standard deviation	± 25.544	± 23.177	-
Treadmill Exercise Time			
Only 84 participants in the placebo arm with available data were analyzed.			
Units: min			
arithmetic mean	12.88	13.60	
standard deviation	± 4.641	± 4.317	-

End points

End points reporting groups

Reporting group title	Eleclazine 30/3/6 mg
Reporting group description:	
Single loading dose of eleclazine 30 mg (5 x 6 mg tablets) on Day 1, followed by 3 mg (1 x 3 mg tablet) daily maintenance dose until Week 12, then 6 mg (2 x 3 mg tablets) daily maintenance dose from Week 12 to at least Week 24	
Reporting group title	Placebo
Reporting group description:	
Placebo tablet (s) administered orally for at least 24 weeks	

Primary: Change in Peak Oxygen Uptake (VO2) Achieved During Cardiopulmonary Exercise Testing (CPET) From Baseline to Week 24

End point title	Change in Peak Oxygen Uptake (VO2) Achieved During Cardiopulmonary Exercise Testing (CPET) From Baseline to Week 24
End point description:	
Full Analysis Set: all randomized participants who received at least 1 dose of study drug. Participants in the Full Analysis Set with available data were analyzed.	
End point type	Primary
End point timeframe:	
Baseline to Week 24	

End point values	Eleclazine 30/3/6 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	68		
Units: mL/kg/min				
arithmetic mean (standard deviation)	0.15 (± 4.312)	0.48 (± 4.143)		

Statistical analyses

Statistical analysis title	Change in Peak VO2- Comparison of Groups
Statistical analysis description:	
The analysis evaluated the change in Peak VO2 from baseline to Week 24 for the eleclazine group compared with that of the placebo group using analysis of covariance (ANCOVA) including terms for baseline Peak VO2, sex, and age (continuous).	
Comparison groups	Placebo v Eleclazine 30/3/6 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.416 [1]
Method	ANCOVA
Parameter estimate	LS Mean Difference(Eleclazine - Placebo)
Point estimate	-0.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.87
upper limit	0.78

Notes:

[1] - P-value and Least Squares (LS) Means are from model with terms for sex, age (continuous), and treatment group and baseline peak VO2 as the covariate.

Secondary: Change in Peak Oxygen Uptake (VO2) Achieved During Cardiopulmonary Exercise Testing (CPET) From Baseline to Week 12

End point title	Change in Peak Oxygen Uptake (VO2) Achieved During Cardiopulmonary Exercise Testing (CPET) From Baseline to Week 12

End point description:

Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Eleclazine 30/3/6 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	78		
Units: mL/kg/min				
arithmetic mean (standard deviation)	0.28 (± 4.028)	0.57 (± 4.314)		

Statistical analyses

Statistical analysis title	Change in Peak VO2- Comparison of Groups

Statistical analysis description:

The analysis evaluated the change in Peak VO2 from baseline to Week 12 for the eleclazine group compared with that of the placebo group using ANCOVA including terms for baseline Peak VO2, sex, and age (continuous).

Comparison groups	Eleclazine 30/3/6 mg v Placebo
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.517 [2]
Method	ANCOVA
Parameter estimate	LS Mean Difference(Eleclazine − Placebo)
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	0.85

Notes:

[2] - P-value and LS Means are from model with terms for sex, age (continuous), and treatment group and baseline peak VO2 as the covariate.

Secondary: Change in Minnesota Living With Heart Failure Questionnaire (MLHFQ) From Baseline to Week 24

End point title	Change in Minnesota Living With Heart Failure Questionnaire (MLHFQ) From Baseline to Week 24

End point description:

The MLHFQ is a 21-item quality of life questionnaire that measures the effects of symptoms, functional limitations, and psychological distress on an individual. Each item is measured on a 6-point Likert scale (0 to 5) and is scored by summing the responses to all 21 questions.

Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Eleclazine 30/3/6 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	73		
Units: Score				
arithmetic mean (standard deviation)	-4.05 (± 15.164)	-5.57 (± 14.345)		

Statistical analyses

Statistical analysis title	Change in MLHFQ- Comparison of Groups

Statistical analysis description:

The analysis evaluated the change in MLHFQ from baseline to Week 24 for the eleclazine group compared with that of the placebo group using ANCOVA including terms for baseline MLHFQ score, sex, and age (continuous).

Comparison groups	Eleclazine 30/3/6 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.513 [3]
Method	ANCOVA
Parameter estimate	LS Mean Difference(Eleclazine - Placebo)
Point estimate	1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.11
upper limit	6.19

Notes:

[3] - P-value and LS Means are from model with terms for sex, age (continuous), and treatment group and baseline score as the covariate.

Secondary: Change in Minnesota Living With Heart Failure Questionnaire (MLHFQ) From Baseline to Week 12

End point title	Change in Minnesota Living With Heart Failure Questionnaire (MLHFQ) From Baseline to Week 12

End point description:

The MLHFQ is a 21-item quality of life questionnaire that measures the effects of symptoms, functional limitations, and psychological distress on an individual. Each item is measured on a 6-point Likert scale (0 to 5) and is scored by summing the responses to all 21 questions. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Eleclazine 30/3/6 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	80		
Units: min				
arithmetic mean (standard deviation)	-3.84 (± 15.654)	-3.40 (± 13.780)		

Statistical analyses

Statistical analysis title	Change in MLHFQ- Comparison of Groups

Statistical analysis description:

The analysis evaluated the change in MLHFQ from baseline to Week 12 for the eleclazine group compared with that of the placebo group using ANCOVA including terms for baseline MLHFQ score, time, sex, and
age (continuous).

Comparison groups	Eleclazine 30/3/6 mg v Placebo
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.964 [4]
Method	ANCOVA
Parameter estimate	LS Mean Difference(Eleclazine − Placebo)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.36
upper limit	4.56

Notes:

[4] - P-value and LS Means are from model with terms for sex, age (continuous), and treatment group and baseline score as the covariate.

Secondary: Change in Treadmill Exercise Time From Baseline to Week 24

End point title	Change in Treadmill Exercise Time From Baseline to Week 24

End point description:

Treadmill exercise time is the time to peak exercise. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Eleclazine 30/3/6 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	68		
Units: min				
arithmetic mean (standard deviation)	0.27 (± 3.954)	0.24 (± 3.208)		

Statistical analyses

Statistical analysis title	Treadmill Exercise Time- Comparison of Groups

Statistical analysis description:

The analysis evaluated the change in treadmill exercise time from baseline to Week 24 for the eleclazine group compared with that of the placebo group using ANCOVA including terms for baseline treadmill exercise time, sex, and age (continuous).

Comparison groups	Eleclazine 30/3/6 mg v Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.944 [5]
Method	ANCOVA
Parameter estimate	LS Mean Difference(Eleclazine - Placebo)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	1.1

Notes:

[5] - P-value and LS Means are from model with terms for sex, age (continuous), and treatment group and baseline treadmill time as the covariate.

Secondary: Change in Treadmill Exercise Time From Baseline to Week 12

End point title	Change in Treadmill Exercise Time From Baseline to Week 12

End point description:

Treadmill exercise time is the time to peak exercise. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Eleclazine 30/3/6 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	77		
Units: min				
arithmetic mean (standard deviation)	0.48 (± 3.295)	0.38 (± 3.030)		

Statistical analyses

Statistical analysis title	Treadmill Exercise Time- Comparison of Groups

Statistical analysis description:

The analysis evaluated the change in treadmill exercise time from baseline to Week 12 for the eleclazine group compared with that of the placebo group using ANCOVA including terms for baseline treadmill exercise time, sex, and age (continuous)

Comparison groups	Eleclazine 30/3/6 mg v Placebo
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.993 [6]
Method	ANCOVA
Parameter estimate	LS Mean Difference(Eleclazine - Placebo)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.97

Notes:

[6] - P-value and LS Means are from model with terms for sex, age (continuous), and treatment group and baseline treadmill time as the covariate.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to the last dose date plus 30 days (maximum exposure: 668 days)

Adverse event reporting additional description:

Safety Analysis Set: all randomized participants who received at least 1 dose of study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Eleclazine 30/3/6 mg

Reporting group description:

Single loading dose of eleclazine 30 mg (5 x 6 mg tablets) on Day 1, followed by 3 mg (1 x 3 mg tablet) daily maintenance dose until Week 12, then 6 mg (2 x 3 mg tablets) daily maintenance dose from Week 12 to at least Week 24

Reporting group title	Placebo

Reporting group description:

Placebo to match eleclazine administered orally for at least 24 weeks

Serious adverse events	Eleclazine 30/3/6 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 86 (16.28%)	16 / 86 (18.60%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (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			
DRUG HYPERSENSITIVITY			

subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (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			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUICIDE ATTEMPT			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
CARDIAC INDEX DECREASED			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
CLAVICLE FRACTURE			

subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FOOT FRACTURE			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL COMPLICATION			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SCAPULA FRACTURE			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
HYPERTROPHIC CARDIOMYOPATHY			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			
subjects affected / exposed	2 / 86 (2.33%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 86 (2.33%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 86 (0.00%)	3 / 86 (3.49%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	2 / 86 (2.33%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FLUTTER			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE ACUTE			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
SYNCOPE			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
CYSTITIS INTERSTITIAL			

subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URETEROLITHIASIS			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
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			
BACK PAIN			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
DEVICE RELATED INFECTION			
subjects affected / exposed	2 / 86 (2.33%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

DIVERTICULITIS			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENDOCARDITIS			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (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 / 86 (1.16%)	0 / 86 (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	1 / 86 (1.16%)	0 / 86 (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	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
HYPOKALAEMIA			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Eleclazine 30/3/6 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 86 (67.44%)	62 / 86 (72.09%)	
Cardiac disorders			
PALPITATIONS			
subjects affected / exposed	9 / 86 (10.47%)	11 / 86 (12.79%)	
occurrences (all)	10	11	
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	2 / 86 (2.33%)	5 / 86 (5.81%)	
occurrences (all)	3	5	
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 86 (0.00%)	6 / 86 (6.98%)	
occurrences (all)	0	7	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	12 / 86 (13.95%)	14 / 86 (16.28%)	
occurrences (all)	14	16	
HEADACHE			
subjects affected / exposed	11 / 86 (12.79%)	11 / 86 (12.79%)	
occurrences (all)	12	12	
PRESYNCOPE			
subjects affected / exposed	5 / 86 (5.81%)	8 / 86 (9.30%)	
occurrences (all)	6	10	
HYPOAESTHESIA			
subjects affected / exposed	1 / 86 (1.16%)	5 / 86 (5.81%)	
occurrences (all)	1	5	
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	11 / 86 (12.79%)	9 / 86 (10.47%)	
occurrences (all)	13	10	

FATIGUE			
subjects affected / exposed	9 / 86 (10.47%)	7 / 86 (8.14%)	
occurrences (all)	10	8	
CHEST DISCOMFORT			
subjects affected / exposed	6 / 86 (6.98%)	3 / 86 (3.49%)	
occurrences (all)	7	5	
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	11 / 86 (12.79%)	11 / 86 (12.79%)	
occurrences (all)	13	13	
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	16 / 86 (18.60%)	8 / 86 (9.30%)	
occurrences (all)	17	8	
COUGH			
subjects affected / exposed	7 / 86 (8.14%)	5 / 86 (5.81%)	
occurrences (all)	7	5	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	5 / 86 (5.81%)	2 / 86 (2.33%)	
occurrences (all)	5	2	
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	9 / 86 (10.47%)	6 / 86 (6.98%)	
occurrences (all)	10	9	
ARTHRALGIA			
subjects affected / exposed	4 / 86 (4.65%)	7 / 86 (8.14%)	
occurrences (all)	4	7	
MUSCLE SPASMS			
subjects affected / exposed	5 / 86 (5.81%)	6 / 86 (6.98%)	
occurrences (all)	5	6	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 86 (0.00%)	5 / 86 (5.81%)	
occurrences (all)	0	5	
Infections and infestations			

UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	7 / 86 (8.14%)	10 / 86 (11.63%)	
occurrences (all)	10	11	
NASOPHARYNGITIS			
subjects affected / exposed	5 / 86 (5.81%)	11 / 86 (12.79%)	
occurrences (all)	6	13	
INFLUENZA			
subjects affected / exposed	3 / 86 (3.49%)	5 / 86 (5.81%)	
occurrences (all)	3	8	
BRONCHITIS			
subjects affected / exposed	1 / 86 (1.16%)	5 / 86 (5.81%)	
occurrences (all)	1	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2015	1) Revision to Inclusion criterion to include adults with baseline Peak VO2 <80% of predicted (rather than <75%) 2) Revision to Predicted Peak VO2 equation 3) For adults screening under Protocol Amendment 1 (10 October 2014), the screening period will be extended to up to 60 days.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 December 2016	A letter was sent to all Study GS-US-361-1157 participating investigators on 18 November 2016, advising them of an important finding identified in a Phase 2 study in participants with ventricular tachycardia/ventricular fibrillation (VT/VF) and implantable cardioverter-defibrillator (ICDs) (Study GS-US-356-0101, TEMPO) in which the incidence rate of ICD shocks was higher in participants who received eleclazine compared with placebo. Another letter was sent to all Study GS-US-361-1157 participating investigators on 13 December 2016, advising them of Gilead's decision to discontinue the development of eleclazine and terminate this study. In light of the data reviewed from Study GS-US-356-0101 and the subsequent discontinuation of the VT/VF development program, the totality of the data did not support continuation of the eleclazine development program for all other indications. This study was terminated prior to the end of the double-blind phase, and therefore no participants entered the open-label extension (OLE) period.	-

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26915375