Clinical trial results:
A Phase 2b, Double-Blind, Placebo-Controlled, Multinational, Multicenter, Randomized Study Evaluating the Safety and Efficacy of Intracoronary Administration of MYDICAR® (AAV1/SERCA2a) in Subjects with Heart Failure

Summary

EudraCT number	2012-001700-37
Trial protocol	SE DE GB BE PL NL DK HU
Global end of trial date	26 February 2016

Results information

Result version number	v1 (current)
This version publication date	06 January 2018
First version publication date	06 January 2018

Trial information

Trial identification

Sponsor protocol code	CELL-004

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Celladon Corporation
Sponsor organisation address	12707 High Bluff Drive, Suite 200, San Diego, United States, 92130
Public contact	Vice President, Clinical Operations, Celladon Corporation, 1 858-432-7217 , jrudy@celladon.net
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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	26 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 February 2015
Global end of trial reached?	Yes
Global end of trial date	26 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of a single intracoronary infusion of 1 x 10*13 DNase Resistant Particles (DRP) MYDICAR® (AAV1/SERCA2a) added to an optimal heart failure (HF) regimen in subjects with ischemic or non-ischemic cardiomyopathy and moderate to advanced symptoms of HF by reducing the frequency of and/or delaying HF-related hospitalizations and episodes of ambulatory worsening HF (recurrent events) compared to placebo-treated subjects.

Protection of trial subjects:

All subjects provided written informed consent and the study was conducted according to the principles of the International Council on Harmonisation Guideline on Good Clinical Practice and the principles of the World Medical Association Declaration of Helsinki. All relevant approvals from Institutional Review Boards or Institutional Ethics Committees were obtained.
Only subjects that met all study inclusion criteria and none of the exclusion criteria were entered in the study. A subject could withdraw consent to participate in the study at any time without prejudice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Sweden: 15
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	United States: 163
Country: Number of subjects enrolled	Israel: 8
Worldwide total number of subjects	250
EEA total number of subjects	79

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)	162
From 65 to 84 years	88
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 55 sites in the US, Israel and the EU including Sweden, UK, Denmark, Poland, Germany, Hungary, Belgium, and the Netherlands.

Pre-assignment

Screening details:

From 09-Jul-2012 through 05-Feb-2014, 1558 subjects at 67 of the 69 initiated sites were pre-screened for adeno-associated virus serotype 1 neutralizing antibodies. Of the 1558 subjects pre-screened, 353 were further screened at 60 sites, of which 250 at 55 sites were ultimately randomized into the trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received a single intracoronary administration of placebo.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intracoronary use

Dosage and administration details:

Placebo was administered via antegrade epicardial coronary artery infusion. Intravenous nitroglycerin was administered before and during placebo infusion, with up-titration based on systolic blood pressure. Infusion of placebo was tailored to the subject’s coronary anatomy and multiple infusion scenarios were possible depending on the extent and distribution of coronary artery stenoses, collateralization patterns and anatomic variations. Operators were instructed that in most cases it was expected that up to 3 infusions should be performed to capture the largest portion of left ventricular blood flow.

Arm title	MYDICAR

Arm description:

Subjects received a single intracoronary administration of MYDICAR.

Arm type	Experimental
Investigational medicinal product name	MYDICAR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intracoronary use

Dosage and administration details:

MYDICAR (1 x 10*13 DNase resistant particles) was administered via antegrade epicardial coronary artery infusion. Intravenous nitroglycerin was administered before and during MYDICAR infusion, with up-titration based on systolic blood pressure.
Infusion of MYDICAR was tailored to the subject’s coronary anatomy and multiple infusion scenarios were possible depending on the extent and distribution of coronary artery stenoses, collateralization patterns and anatomic variations. Operators were instructed that in most cases it was expected that up to 3 infusions should be performed to capture the largest portion of left ventricular blood flow.

Number of subjects in period 1	Placebo	MYDICAR
Started	127	123
Completed	101	98
Not completed	26	25
Agreed to phone follow-up only	4	2
Consent withdrawn by subject	1	2
Death	12	16
Heart transplant	3	3
Unspecified	1	-
Mechanical circulatory support device	5	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single intracoronary administration of placebo.	
Reporting group title	MYDICAR
Reporting group description:	
Subjects received a single intracoronary administration of MYDICAR.	

Reporting group values	Placebo	MYDICAR	Total
Number of subjects	127	123	250
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	58.5	60.4	
standard deviation	± 12.33	± 9.73	-
Gender categorical			
Units: Subjects			
Female	25	21	46
Male	102	102	204

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received a single intracoronary administration of placebo.	
Reporting group title	MYDICAR
Reporting group description:	
Subjects received a single intracoronary administration of MYDICAR.	
Subject analysis set title	Modified intention-to-treat population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized subjects who received the investigational medicinal product.	

Primary: Recurrent heart failure-related hospitalizations and worsening heart failure

End point title	Recurrent heart failure-related hospitalizations and worsening heart failure
End point description:	
The primary efficacy endpoint was the time to recurrent events (hospitalizations related to failure of the native heart that was not implanted with a mechanical circulatory support device [MCSD; left, right or biventricular assist device, total artificial heart] and ambulatory worsening failure of the native heart that was not implanted with an MCSD in the presence of terminal events (all-cause death, heart transplant, MCSD implantation) based on the joint frailty model.	
End point type	Primary
End point timeframe:	
Clinical events were collected until the Primary Analysis Data Cutoff was reached which was when all subjects had completed the 12-month Active Observation Period, or terminated early and at least 186 adjudicated primary endpoints had occurred in the ITT.	

End point values	Placebo	MYDICAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	121		
Units: Recurrent event rate (per patient-year)				
number (not applicable)	0.74	0.63		

Statistical analyses

Statistical analysis title	Hazard ratio analysis
Comparison groups	Placebo v MYDICAR

Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.65

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The reporting period for treatment-emerging adverse events started on the day of infusion with the investigational medicinal product (Day 0) and ended when a subject completed the 12-month active observation period or was terminated from the study.

Adverse event reporting additional description:

Non-serious adverse events were not analyzed separately; therefore, the list of non-serious adverse events also includes serious adverse events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received a single intracoronary administration of placebo.

Reporting group title	MYDICAR

Reporting group description:

Subjects received a single intracoronary administration of MYDICAR.

Serious adverse events	Placebo	MYDICAR	
Total subjects affected by serious adverse events			
subjects affected / exposed	72 / 122 (59.02%)	71 / 121 (58.68%)	
number of deaths (all causes)	20	25	
number of deaths resulting from adverse events			
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haematoma			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	4 / 122 (3.28%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous insufficiency			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cardiac ablation			
subjects affected / exposed	1 / 122 (0.82%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker insertion			
subjects affected / exposed	0 / 122 (0.00%)	3 / 121 (2.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac resynchronisation therapy			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary arterial stent insertion			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart transplant			

subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implantable defibrillator insertion			
subjects affected / exposed	6 / 122 (4.92%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device battery replacement			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device change			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Percutaneous coronary intervention			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurodesis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth extraction			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular assist device insertion			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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			
Adverse drug reaction			

subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 122 (0.00%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
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	6 / 122 (4.92%)	4 / 121 (3.31%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device lead issue			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site oedema			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
medical device complication			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis			

subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	1 / 122 (0.82%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Sudden death			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Asthma			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 122 (0.00%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	5 / 122 (4.10%)	4 / 121 (3.31%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 10	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	0 / 122 (0.00%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
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 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			

subjects affected / exposed	0 / 122 (0.00%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
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	0 / 122 (0.00%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Arthroscopy			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood magnesium decreased			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			

subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate increased			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scan abnormal			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant evaluation			
subjects affected / exposed	0 / 122 (0.00%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Cardiac valve rupture			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			

subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	3 / 122 (2.46%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 122 (1.64%)	6 / 121 (4.96%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	2 / 122 (1.64%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			

subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 122 (0.00%)	4 / 121 (3.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 3	
Cardiac failure			
subjects affected / exposed	23 / 122 (18.85%)	25 / 121 (20.66%)	
occurrences causally related to treatment / all	0 / 45	0 / 44	
deaths causally related to treatment / all	0 / 5	0 / 4	
Cardiac failure acute			
subjects affected / exposed	6 / 122 (4.92%)	11 / 121 (9.09%)	
occurrences causally related to treatment / all	0 / 12	0 / 16	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	12 / 122 (9.84%)	8 / 121 (6.61%)	
occurrences causally related to treatment / all	0 / 39	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiogenic shock			
subjects affected / exposed	2 / 122 (1.64%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiomegaly			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			

subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mitral valve disease			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Palpitations			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular failure			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	2 / 122 (1.64%)	3 / 121 (2.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			

subjects affected / exposed	6 / 122 (4.92%)	5 / 121 (4.13%)	
occurrences causally related to treatment / all	0 / 13	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Convulsion			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Syncope			
subjects affected / exposed	4 / 122 (3.28%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Amaurosis Fugax			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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	2 / 122 (1.64%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis relapsing			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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	2 / 122 (1.64%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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			
Nephropathy			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 122 (1.64%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure acute			
subjects affected / exposed	6 / 122 (4.92%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Gouty arthritis			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			

subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	3 / 122 (2.46%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 122 (0.82%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			

subjects affected / exposed	5 / 122 (4.10%)	4 / 121 (3.31%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Postoperative wound infection			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			

subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	MYDICAR	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	111 / 122 (90.98%)	111 / 121 (91.74%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	9 / 122 (7.38%)	11 / 121 (9.09%)	
occurrences (all)	15	11	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	4 / 122 (3.28%)	8 / 121 (6.61%)	
occurrences (all)	4	11	
Cardiac failure			
subjects affected / exposed	29 / 122 (23.77%)	31 / 121 (25.62%)	
occurrences (all)	57	58	
Cardiac failure acute			
subjects affected / exposed	6 / 122 (4.92%)	11 / 121 (9.09%)	
occurrences (all)	12	16	

Cardiac failure congestive			
subjects affected / exposed	13 / 122 (10.66%)	10 / 121 (8.26%)	
occurrences (all)	42	10	
Ventricular tachycardia			
subjects affected / exposed	9 / 122 (7.38%)	10 / 121 (8.26%)	
occurrences (all)	17	14	
Surgical and medical procedures			
Implantable defibrillator insertion			
subjects affected / exposed	7 / 122 (5.74%)	0 / 121 (0.00%)	
occurrences (all)	7	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 122 (6.56%)	9 / 121 (7.44%)	
occurrences (all)	8	9	
Syncope			
subjects affected / exposed	7 / 122 (5.74%)	2 / 121 (1.65%)	
occurrences (all)	10	2	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 122 (3.28%)	7 / 121 (5.79%)	
occurrences (all)	4	8	
Chest pain			
subjects affected / exposed	7 / 122 (5.74%)	8 / 121 (6.61%)	
occurrences (all)	8	10	
Fatigue			
subjects affected / exposed	7 / 122 (5.74%)	8 / 121 (6.61%)	
occurrences (all)	8	8	
Oedema peripheral			
subjects affected / exposed	2 / 122 (1.64%)	7 / 121 (5.79%)	
occurrences (all)	2	7	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 122 (5.74%)	4 / 121 (3.31%)	
occurrences (all)	7	5	
Nausea			

subjects affected / exposed	11 / 122 (9.02%)	6 / 121 (4.96%)	
occurrences (all)	11	7	
Vomiting			
subjects affected / exposed	7 / 122 (5.74%)	4 / 121 (3.31%)	
occurrences (all)	7	4	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	12 / 122 (9.84%)	9 / 121 (7.44%)	
occurrences (all)	14	11	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	9 / 122 (7.38%)	5 / 121 (4.13%)	
occurrences (all)	10	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 122 (3.28%)	7 / 121 (5.79%)	
occurrences (all)	4	7	
Infections and infestations			
Bronchitis			
subjects affected / exposed	7 / 122 (5.74%)	5 / 121 (4.13%)	
occurrences (all)	7	6	
Pneumonia			
subjects affected / exposed	8 / 122 (6.56%)	7 / 121 (5.79%)	
occurrences (all)	8	7	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	8 / 122 (6.56%)	6 / 121 (4.96%)	
occurrences (all)	9	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2012	Exclusion criterion #10 was removed and text added as a new expanded section, "Section 4.3 Contraindications for Infusion of Investigational Medicinal Product". Exclusion criterion #15 was added to exclude subjects with current history of malignancy except for basal cell carcinoma. The collection of biopsies or specimens of myocardial tissue was added, if a subject received a left ventricular assist device or transplant, for qPCR analysis to determine presence of the vector transgene. "Section 7.15 Clinical Events" was added.
14 February 2013	Inclusion Criterion #2 was changed to exclude hypertrophic cardiomyopathy and include toxic and alcoholic myopathies if sufficient time had elapsed to rule out spontaneous recovery. Inclusion Criterion #5 was changed to include New York Heart Association Class II. Inclusion Criterion #6 was changed to specify that optimized HF therapy was to also be 'individualized' and 'appropriate to the individual subject'. Inclusion Criterion #9 was added, which required all subjects to have a risk factor of either hospitalization within 6 months of Screening or elevated N-terminal prohormone brain natriuretic peptide/B-Type natriuretic peptide within 30 days of Screening. Inclusion Criterion #10 was added regarding angiography. Exclusion Criterion #2 was changed to include acute myocarditis. Exclusion Criterion #13 was changed to define anemia as hemoglobin ≤9g/dL provided there was no evidence of bleeding. Exclusion Criterion #15 was changed to specify "Diagnosis of, or treatment for, any cancer other than basal cell carcinoma within the last 5 years." The end of study and Primary Analysis Date Cutoff definitions were changed. "Discontinuation of the Study" was changed to "Discontinuation of Enrollment" and the reasons for discontinuing enrollment were restricted to the recommendation of the Data Monitoring Committee or in the event of bankruptcy. Study medication storage conditions were updated for unopened vials to include 2-8°C for up to 3 months. The table of "Commercially Available MYDICAR Device Delivery Products" was expanded.
21 October 2013	The number of subjects was increased from 200 to 250 (from 100 to 125 per treatment group) and the number of required primary endpoints was increased from 180 to 186 in order to declare the Primary Analysis Date Cutoff. Appendix L was added to describe hospitalization and biohazard handling procedures in Hungary.
18 March 2014	The duration of follow-up of subjects was extended from 2 to 5 years with the addition of the Extended Long-Term Follow-Up Period which encompassed quarterly telephonic visits.
01 December 2014	The modified intention-to-treat (mITT) population (randomized subjects who received study medication) was defined as the analysis population for the primary efficacy analysis. The mITTx analysis population was added, which excluded subjects who were adeno-associated virus serotype 1 neutralizing antibody positive or equivocal 1:2 at Baseline.
11 June 2015	The extended long-term follow-up (LT-FUP) was eliminated. LT-FUP quarterly visits were changed to telephone calls and collection of health status only. Tissue collection was eliminated. The collection of clinical events in the LT-FUP was eliminated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported