



Clinical trial results:

CXCR4 Antagonism for Cell Mobilisation and Healing in Acute Myocardial Infarction (CATCH-AMI)

A Phase IIa, Double-Blind, Placebo-Controlled, Randomised, Multi-centre Study of POL6326, a CXCR4 Antagonist, in Patients with Large Reperfused ST-Elevation Myocardial Infarction

Summary

EudraCT number	2012-003229-91
Trial protocol	DE GB AT HU PL CZ NO HR
Global end of trial date	06 August 2015

Results information

Result version number	v1 (current)
This version publication date	20 August 2016
First version publication date	20 August 2016

Trial information

Trial identification

Sponsor protocol code	POL6326-POL-006
-----------------------	-----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01905475
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Polyphor AG
Sponsor organisation address	Hegenheimermattweg 125, Allschwil, Switzerland, 4123
Public contact	Dr. med. Klaus Dembowsky, Polyphor AG, +41 61567 1641, Klaus.Dembowsky@polyphor.com
Scientific contact	Dr. med. Klaus Dembowsky, Polyphor AG, +41 61567 1641, Klaus.Dembowsky@polyphor.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	20 April 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 August 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the effects of the CXCR4 antagonist POL6326 on cardiac function and infarct size in patients with large reperfused STEMI.

Protection of trial subjects:

Independent Data Monitoring Committee

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 August 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Austria: 24
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 43
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	82
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 213 patients were recruited for the study at 16 out of 25 initiated centres between August 2013 and August 2015.

Of the 120 patients entered into the double-blind phase, 60 were randomised to receive POL6326 1.5 mg/kg and 60 to receive placebo.

Pre-assignment

Screening details:

This study included a pre-study and screening phase up to 4 days prior to the treatment phase. To help minimize screen failures, patients were to have had an assessment of their LV function during the pre-study phase to obtain a first estimate of LVEF following their PCI in line with the site's standard-of-care.

Pre-assignment period milestones

Number of subjects started	213 ^[1]
Number of subjects completed	120

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Failure to meet inclusion criteria: 93
----------------------------	--

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 213 patients were recruited for the study, 93 were screen failures (failure to meet inclusion criteria).

Period 1

Period 1 title	Overall trial (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
Arm title	POL6326 1.5 mg/kg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	POL6326
Investigational medicinal product code	POL6326
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.5 mg/kg POL6326 administered as a 2-hour IV infusion, on treatment Days 1 and 3

Arm title	Placebo
------------------	---------

Arm description: -

Arm type	Placebo
Investigational medicinal product name	POL6326 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Number of subjects in period 1	POL6326 1.5 mg/kg	Placebo
Started	60	60
Intent to Treat (ITT) Population	60	60
Modified ITT Population	55	59
Per Protocol Population	48	56
Safety Population	60	60
Completed	31	28
Not completed	29	32
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-
Death	1	1
Other	26	30
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	POL6326 1.5 mg/kg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	POL6326 1.5 mg/kg	Placebo	Total
Number of subjects	60	60	120
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	57.7	58.5	
standard deviation	± 10.56	± 12.08	-
Gender categorical			
Units: Subjects			
Female	17	8	25
Male	43	52	95
LVEF (%)			
Left ventricular ejection fraction (%)			
Units: Subjects			
< Median: 38.0 (%)	29	29	58
>= Median: 38.0 (%)	31	30	61
Missing	0	1	1
LVEDV Index			
Left ventricular end-diastolic volume index			
Units: Subjects			
< Median: 87.5	35	24	59
>= Median: 87.5	25	34	59
Missing	0	2	2
LVESV Index			
Left ventricular end-systolic volume index			
Units: Subjects			
< Median: 53.0	28	25	53
>= Median: 53.0	32	33	65
Missing	0	2	2

Infarct Size			
Units: Subjects			
< Median: 28.0	29	24	53
>= Median: 28.0	28	31	59
Missing	3	5	8
NT-proBNP Level (pg/ml)			
N-terminal pro-B-type natriuretic peptide level			
Units: Subjects			
< Median: 2000.0 (pg/ml)	28	31	59
>= Median: 2000.0 (pg/ml)	31	28	59
Missing	1	1	2
Growth Differentiation Factor-15 (pg/ml)			
Units: Subjects			
< Median: 1319.0 (pg/ml)	25	34	59
>= Median: 1319.0 (pg/ml)	34	25	59
Missing	1	1	2
High-sensitivity Troponin T (pg/ml)			
Units: Subjects			
< Median: 3631.0 (pg/ml)	30	29	59
>= Median: 3631.0 (pg/ml)	29	30	59
Missing	1	1	2
Microvascular Obstruction			
Units: Subjects			
Present	43	45	88
Not Present	17	14	31
Missing	0	1	1
Cardiovascular Examination			
Units: Subjects			
Normal	50	53	103
Abnormal, NCS	7	7	14
Abnormal, CS	3	0	3
Complicated PCI Procedure			
Units: Subjects			
Yes	8	6	14
No	52	54	106
PCI Vessel Placement			
Multiple entries could be recorded for a patient			
Units: Subjects			
Left mainstem	1	1	2
Left anterior descending artery	44	45	89
Circumflex	6	4	10
Right coronary artery	6	5	11
Multiple PCI	3	5	8
Type of Stent			
Multiple entries could be recorded for a patient			
Units: Subjects			
Bare-metal	19	19	38
Drug eluting	37	40	77
Both	4	1	5

Time from Onset of AMI Symptoms to Reperfusion			
Calculated as [(date and time of reperfusion minus date and time of onset of AMI symptoms) divided by 3600]			
Units: hour			
arithmetic mean	10.19	8.69	
standard deviation	± 14.139	± 10.094	-
Time from Onset of AMI Symptoms to Start of First Treatment			
Calculated as [(date and time of start of first treatment minus date and time of onset of AMI symptoms) divided by 86400]			
Units: day			
arithmetic mean	4.22	3.95	
standard deviation	± 0.76	± 0.556	-
Time from Reperfusion to Start of First Treatment			
Calculated as [(date and time of start of first treatment minus date and time of reperfusion) divided by 3600]			
Units: hour			
arithmetic mean	90.4	85.8	
standard deviation	± 12.636	± 12.577	-

End points

End points reporting groups

Reporting group title	POL6326 1.5 mg/kg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	ITT- POL6326 1.5 mg/kg
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomised patients were included in the Intent-to-Treat (ITT) population. Patients were analysed according to the randomised treatment.	
Subject analysis set title	ITT - Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomised patients were included in the Intent-to-Treat (ITT) population. Patients were analysed according to the randomised treatment.	
Subject analysis set title	MITT- POL6326 1.5 mg/kg
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All randomised and treated patients with matching MRI measurements at baseline and at 4 months. Patients were analysed according to the randomised treatment.	
Subject analysis set title	MITT - Placebo
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All randomised and treated patients with matching MRI measurements at baseline and at 4 months. Patients were analysed according to the randomised treatment.	
Subject analysis set title	Per-Protocol- POL6326 1.5 mg/kg
Subject analysis set type	Per protocol
Subject analysis set description: All patients in the MITT population without important protocol deviations, dosed as per the treatment arm to which they were randomised, and received both treatment infusions.	
Subject analysis set title	Per-Protocol - Placebo
Subject analysis set type	Per protocol
Subject analysis set description: All patients in the MITT population without important protocol deviations, dosed as per the treatment arm to which they were randomised, and received both treatment infusions.	
Subject analysis set title	Safety Population- POL6326 1.5 mg/kg
Subject analysis set type	Safety analysis
Subject analysis set description: All randomised patients who received at least one dose of study drug. Patients were analysed according to the treatment they actually received.	
Subject analysis set title	Safety Population - Placebo
Subject analysis set type	Safety analysis
Subject analysis set description: All randomised patients who received at least one dose of study drug. Patients were analysed according to the treatment they actually received.	

Primary: change from baseline of global LVEF

End point title	change from baseline of global LVEF
End point description: The primary efficacy analysis was the comparison of the change from baseline of global LVEF to the 4-Month visit between POL6326 versus placebo based on the MITT. Hypothesis testing for a potential	

superiority of POL6326 was performed with a two-sided hypothesis testing.

End point type	Primary
End point timeframe:	
At base line (day 2 or 3) and 4 months	

End point values	MITT- POL6326 1.5 mg/kg	MITT - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	59		
Units: percent				
arithmetic mean (standard error)	7.27 (\pm 1.227)	5.56 (\pm 1.316)		

Statistical analyses

Statistical analysis title	LS Mean Differences from Placebo
Statistical analysis description:	
Post-baseline LS means, LS mean differences, 95% CI for differences and p-values were from ANCOVA model with treatment as fixed factor and baseline and gender as covariates.	
Comparison groups	MITT- POL6326 1.5 mg/kg v MITT - Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.289
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.47
upper limit	4.89
Variability estimate	Standard error of the mean
Dispersion value	1.606

Secondary: Change in infarct size

End point title	Change in infarct size
End point description:	
End point type	Secondary
End point timeframe:	
At base line (day 2 or 3) and 4 months	

End point values	MITT- POL6326 1.5 mg/kg	MITT - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	51		
Units: percent				
arithmetic mean (standard deviation)	-7.5 (± 9.43)	-7 (± 10.1)		

Statistical analyses

Statistical analysis title	LS Mean Differences from Placebo
Statistical analysis description:	
Post-baseline LS means, LS mean differences, 95% CI for differences and p-values were from ANCOVA model with treatment as fixed factor and baseline and gender as covariates.	
Comparison groups	MITT - Placebo v MITT- POL6326 1.5 mg/kg
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.717
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.83
upper limit	2.64
Variability estimate	Standard error of the mean
Dispersion value	1.631

Secondary: Change in LVEDV index

End point title	Change in LVEDV index
End point description:	
End point type	Secondary
End point timeframe:	
At base line (day 2 or 3) and 4 months	

End point values	MITT- POL6326 1.5 mg/kg	MITT - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	58		
Units: percent				
arithmetic mean (standard deviation)	5.3 (± 21.36)	6.4 (± 18.5)		

Statistical analyses

Statistical analysis title	LS Mean Differences from Placebo
Statistical analysis description: Only patients who had both baseline and post-baseline values are included	
Comparison groups	MITT- POL6326 1.5 mg/kg v MITT - Placebo
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.724
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.29
upper limit	5.77
Variability estimate	Standard error of the mean
Dispersion value	3.547

Notes:

[1] - Post-baseline LS means, LS mean differences, 95% CI for differences and p-values were from ANCOVA model with treatment as fixed factor and baseline and gender as covariates.

Secondary: Change in LVESV index

End point title	Change in LVESV index
End point description:	
End point type	Secondary
End point timeframe:	
At base line (day 2 or 3) and 4 months	

End point values	MITT- POL6326 1.5 mg/kg	MITT - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	58		
Units: percent				
arithmetic mean (standard deviation)	-2.3 (\pm 16.78)	0.9 (\pm 18.29)		

Statistical analyses

Statistical analysis title	LS Mean Differences from Placebo
Statistical analysis description:	
Only patients who had both baseline and post-baseline values are included	
Comparison groups	MITT- POL6326 1.5 mg/kg v MITT - Placebo
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.44
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.67
upper limit	3.79
Variability estimate	Standard error of the mean
Dispersion value	3.145

Secondary: Change in regional LV function

End point title	Change in regional LV function
End point description:	
Change in regional left ventricular function	
End point type	Secondary
End point timeframe:	
At base line (day 2 or 3) and 4 months	

End point values	MITT- POL6326 1.5 mg/kg	MITT - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	59		
Units: percent				
arithmetic mean (standard deviation)	0.2 (± 0.8)	0.2 (± 0.85)		

Statistical analyses

Statistical analysis title	LS Mean Differences from Placebo
Statistical analysis description:	
Only patients who had both baseline and post-baseline values are included	
Comparison groups	MITT- POL6326 1.5 mg/kg v MITT - Placebo

Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.872
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.14

Secondary: All-cause mortality

End point title	All-cause mortality
End point description:	
End point type	Secondary
End point timeframe:	
Assessed at 6 weeks and 4 months	

End point values	POL6326 1.5 mg/kg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: day				
median (confidence interval 95%)	350 (350 to 350)	100 (100 to 100)		

Statistical analyses

Statistical analysis title	Hazard Ratio relative to Placebo
Comparison groups	POL6326 1.5 mg/kg v Placebo
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.986
Method	Kaplan-Meier Curves
Parameter estimate	Hazard ratio (HR)
Point estimate	0.723

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	12.944

Secondary: Heart failure hospitalisations

End point title	Heart failure hospitalisations
End point description:	
End point type	Secondary
End point timeframe:	
6 weeks and 4 months	

End point values	POL6326 1.5 mg/kg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: day				
median (confidence interval 95%)	10 (10 to 10)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Time of Informed Consent until 4 months after baseline MRI, or ultimate discharge from the study, whichever comes first.

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

Dictionary used

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

Dictionary version	16.0
--------------------	------

Reporting groups

Reporting group title	POL6326 1.5 mg/kg
-----------------------	-------------------

Reporting group description: -	
--------------------------------	--

Reporting group title	Placebo
-----------------------	---------

Reporting group description:	
------------------------------	--

Placebo	
---------	--

Serious adverse events	POL6326 1.5 mg/kg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 60 (26.67%)	17 / 60 (28.33%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal cancer			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Surgical and medical procedures			
Implantable defibrillator insertion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (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			
Non-cardiac chest pain			
subjects affected / exposed	1 / 60 (1.67%)	3 / 60 (5.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			

subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
International normalised ratio increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (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			
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 60 (1.67%)	2 / 60 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 60 (3.33%)	2 / 60 (3.33%)	
occurrences causally related to treatment / all	1 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	2 / 60 (3.33%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			

subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (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	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 60 (0.00%)	2 / 60 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			

subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
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			
Anaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			

subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (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: 0 %

Non-serious adverse events	POL6326 1.5 mg/kg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 60 (40.00%)	22 / 60 (36.67%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal neoplasm			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Colorectal cancer			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Hypertension			

subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences (all)	1	1	
Intermittent claudication			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	0 / 60 (0.00%)	2 / 60 (3.33%)	
occurrences (all)	0	2	
Phlebitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Implantable defibrillator insertion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	3 / 60 (5.00%)	2 / 60 (3.33%)	
occurrences (all)	3	2	
Feeling hot			
subjects affected / exposed	2 / 60 (3.33%)	1 / 60 (1.67%)	
occurrences (all)	2	1	
Non-cardiac chest pain			
subjects affected / exposed	2 / 60 (3.33%)	3 / 60 (5.00%)	
occurrences (all)	2	3	
Catheter site inflammation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Catheter site pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Device dislocation			

subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Drug ineffective			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Extravasation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Feeling abnormal			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Feeling cold			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 60 (3.33%)	2 / 60 (3.33%)	
occurrences (all)	2	2	
Epistaxis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Throat irritation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	
Pleural effusion subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	
Rales subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	2 / 60 (3.33%) 2	
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	
Psychiatric disorders Suicide attempt subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Depression subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	
Insomnia subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	
Investigations Aspiration bone marrow subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Blood potassium increased subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Haemoglobin decreased subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Hepatic enzyme increased subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
International normalised ratio increased			

subjects affected / exposed	1 / 60 (1.67%)	2 / 60 (3.33%)	
occurrences (all)	1	2	
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Blood bilirubin increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Blood glucose increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Blood urea increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Colonoscopy			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Liver function test abnormal			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Neutrophil count			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
White blood cell count increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 60 (3.33%)	0 / 60 (0.00%)	
occurrences (all)	2	0	
Arthropod bite			

subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Sunburn			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	4 / 60 (6.67%)	2 / 60 (3.33%)	
occurrences (all)	4	2	
Palpitations			
subjects affected / exposed	3 / 60 (5.00%)	0 / 60 (0.00%)	
occurrences (all)	0	0	
Supraventricular extrasystoles			
subjects affected / exposed	3 / 60 (5.00%)	0 / 60 (0.00%)	
occurrences (all)	3	0	
Ventricular extrasystoles			
subjects affected / exposed	3 / 60 (5.00%)	0 / 60 (0.00%)	
occurrences (all)	3	0	
Intracardiac thrombus			
subjects affected / exposed	2 / 60 (3.33%)	0 / 60 (0.00%)	
occurrences (all)	2	0	
Ventricular tachycardia			
subjects affected / exposed	2 / 60 (3.33%)	0 / 60 (0.00%)	
occurrences (all)	2	0	
Acute myocardial infarction			
subjects affected / exposed	1 / 60 (1.67%)	2 / 60 (3.33%)	
occurrences (all)	1	2	
Angina pectoris			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences (all)	1	1	
Atrioventricular block complete			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	

Atrioventricular block second degree		
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)
occurrences (all)	0	0
Bradycardia		
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)
occurrences (all)	1	1
Cardiac flutter		
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)
occurrences (all)	0	0
Coronary artery disease		
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)
occurrences (all)	0	0
Sinus bradycardia		
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)
occurrences (all)	1	0
Sinus tachycardia		
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)
occurrences (all)	1	0
Supraventricular tachycardia		
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)
occurrences (all)	1	1
Acute coronary syndrome		
subjects affected / exposed	0 / 60 (0.00%)	2 / 60 (3.33%)
occurrences (all)	0	2
Angina unstable		
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	1
Arrhythmia		
subjects affected / exposed	0 / 60 (0.00%)	2 / 60 (3.33%)
occurrences (all)	0	2
Atrial fibrillation		
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	1
Coronary artery stenosis		
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	1

Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Cerebrovascular accident			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Paresis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Sensory loss			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Burning sensation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 60 (0.00%)	2 / 60 (3.33%)	
occurrences (all)	0	2	
Hemiparesis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 60 (1.67%)	2 / 60 (3.33%)	
occurrences (all)	1	2	
Diarrhoea			

subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 60 (1.67%)	2 / 60 (3.33%)	
occurrences (all)	1	2	
Haematochezia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Inguinal hernia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	0 / 60 (0.00%)	2 / 60 (3.33%)	
occurrences (all)	0	2	
Flatulence			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Hiatus hernia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Pruritus			

subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 60 (0.00%) 0	
Angioedema subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	1 / 60 (1.67%) 1	
Dermal cyst subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Eczema subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Urticaria subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Haematuria subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	
Polyuria subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	1 / 60 (1.67%) 1	
Back pain subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Bursitis			

subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Exostosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences (all)	1	1	
Myalgia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Spinal osteoarthritis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	2 / 60 (3.33%)	0 / 60 (0.00%)	
occurrences (all)	2	0	
Gastroenteritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Impetigo			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences (all)	1	0	

Respiratory tract infection subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	1 / 60 (1.67%) 1	
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	1 / 60 (1.67%) 1	
Influenza subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	2 / 60 (3.33%) 2	
Metabolism and nutrition disorders			
Glucose tolerance impaired subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	1 / 60 (1.67%) 1	
Gout subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Hyperuricaemia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	2 / 60 (3.33%) 2	
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 60 (0.00%) 0	
Diabetes mellitus subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	2 / 60 (3.33%) 2	
Hyperlipidaemia subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 60 (1.67%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 February 2014	<p>Protocol version 4 dated 14 January 2014 (amendment #3), divided the study period in primary (4-Month visit) and extended (12-Month visit) study periods, clarified the eligibility for patients no longer showing ST-segmental elevation or with previous PCI, decreased the eGFR from 60 mL/minute to 40 mL/minute in the inclusion/exclusion criteria, and described changes to the statistical analysis and to the clinical study report.</p> <p>Amendment #3 also changed the time points for some screening procedures, included the urinalysis to the list of assessments, and changed the pharmacokinetic and pharmacodynamic sampling process and time points based on the analysis of PK/PD data from the first 16 randomised patients. Amendment #3 also allowed different strengths for the MRI scanner (both 1.5T and 3T).</p>
09 July 2014	<p>Protocol version 5 dated 9 May 2014 (amendment # 4) added information specifying the assessments to be performed in the 5 years extended follow-up phase of the study, and described changes to the statistical analysis and to the clinical study report.</p>
09 July 2015	<p>Following the review of efficacy data analysed according to the planned interim analysis, the IDMC recommended to discontinue the enrollment of any additional patients into the study because of futility (i.e., conditional power (CP) $\leq 10\%$). The protocol was therefore amended to continue the trial with the 120 patients enrolled up to that point in time until the Month 4 visits were complete.</p> <p>Protocol version 6 dated 8 June 2015 (amendment #5) removed Month 12 as an outpatient visit and replaced it as a follow-up assessment via a telephone contact to ascertain the patients' health status. In reference to the primary and extended study periods, the 5 years longterm follow-up were also removed. Lastly, the definition of hospitalization was clarified, and the pharmacovigilance provider was changed, and details on additional supportive analysis and endpoints (e.g., high-sensitive troponin T and growth differentiation factor-15 biomarkers) were added. Although protocol version 6 defines study completion as the completion of the Month 4 outpatient visits, 12-Month data collected up to the last Month 4 visit was analysed and included here. Additional exploratory analysis and data collected from the 12-Month telephone contact are intended to be reported in an addendum to the clinical study report.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
02 April 2015	<p>An interim analysis was performed once 50% of the 140 planned patients had completed their 4-month visit and MRI assessment. The IDMC recommended discontinuing further patient recruitment for reasons of futility since the Conditional Power (CP) for success of the trial (defined as the POL6326 arm being superior over the placebo arm for LVEF at 4 months) appeared to be below the lower limit of the pre-defined threshold.</p>	-

Notes:

Limitations and caveats

None reported