Clinical trial results:
A randomized, double-blind multicenter study to assess the safety and efficacy of a six month oral treatment with the chymase inhibitor BAY1142524 at a dose of 25 mg BID in comparison to placebo on top of standard of care in patients with reduced leftventricular ejection fraction (LVEF 45%) after acute myocardial infarction (CHIARA MIA 2)

Summary

EudraCT number	2016-002167-33
Trial protocol	CZ DE ES
Global end of trial date	04 September 2018

Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019

Trial information

Trial identification

Sponsor protocol code	16673

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02976467
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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	04 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objectives:
1. Investigate the change in LVEF from baseline to 6 months after treatment with BAY 1142524 in comparison to placebo and in addition to standard of care therapy, as measured by cardiac MRI.

2. Investigate the change in EDVI from baseline to 6 months after treatment with BAY 1142524 in comparison to placebo and in addition to standard of care as measured by cardiac MRI.

3.Investigate the change in ESVI from baseline to 6 months after treatment with BAY 1142524 in comparison to placebo and in addition to standard of care as measured by cardiac MRI.

Secondary objective:
4. Analyze safety and tolerability of 25 mg of BAY 1142524 BID as evidenced by the incidence and severity of AEs.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy:

Optimized standard of care therapy according to international and/or local guidelines

Evidence for comparator:

Placebo matching to BAY 1142524, 25 mg immediate release tablet

Actual start date of recruitment	12 December 2016
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	Czech Republic: 18
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Israel: 86
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Spain: 24
Worldwide total number of subjects	185
EEA total number of subjects	99

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)	144
From 65 to 84 years	41
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 25 study centers in 5 countries: five study centers in the Czech Republic, four study centers in Germany, six study centers in Israel, five study centers in Italy and five study centers in Spain between 30-Dec2016 (first patient first visit) and 04-Sep-2018 (last patient last visit).

Pre-assignment

Screening details:

A total of 185 subjects were screened in the study, of whom 78 subjects were screen failures.
A total of 107 subjects were randomized in a 1:1 ratio to the BAY 1142524 arm (54 subjects) and the placebo arm (53 subjects).

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	BAY 1142524

Arm description:

Efficacy evaluation was performed in the per protocol set (PPS) and full analysis set (FAS). A total of 42 subjects in the BAY 1142524 arm were valid for the PPS and 54 subjects for the FAS.

Arm type	Experimental
Investigational medicinal product name	BAY 1142524
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg immediate release tablet

Arm title	Placebo

Arm description:

Efficacy evaluation was performed in the per protocol set (PPS) and full analysis set (FAS). A total of 38 subjects in the placebo arm were valid for the PPS and 53 subjects for the FAS.

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 matching to BAY 1142524, 25 mg immediate release tablet

Number of subjects in period 1[1]	BAY 1142524	Placebo
Started	54	53
Completed	47	48
Not completed	7	5
Not completed study	7	4
1 subject without second MRI evaluation	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Number of subjects reported to be in the baseline period represents: Subjects randomized
Number of subjects worldwide represents: Subjects screened / enroled

Subject analysis sets	
Subject analysis set title	BAY 1142524 / LVEF (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in Left ventricular ejection fraction (LVEF) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / EDVI (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in End diastolic volume index (EDVI) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / ESVI (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in End systolic volume index (ESVI) from baseline to 6 months (Day 168) after treatment with BAY 1142524 in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / LVEF (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in Left ventricular ejection fraction (LVEF) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / EDVI (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in End diastolic volume index (EDVI) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / ESVI (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in End systolic volume index (ESVI) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / LVEF (PPS) - Baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
Left ventricular ejection fraction (LVEF) at baseline in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / EDVI (PPS) - Baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
End diastolic volume index (EDVI) at baseline in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / ESVI (PPS) - Baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
End systolic volume index (ESVI) at baseline in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / LVEF (PPS) - Baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
Left ventricular ejection fraction (LVEF) at baseline in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / EDVI (PPS) - Baseline

Subject analysis set type	Per protocol
Subject analysis set description:	
End diastolic volume index (EDVI) at baseline in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / ESVI (PPS) - Baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
End systolic volume index (ESVI) at baseline in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / LVEF (PPS) - Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Left ventricular ejection fraction (LVEF) at day 168 in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / EDVI (PPS) - Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
End diastolic volume index (EDVI) at day 168 in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / ESVI (PPS) - Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
End systolic volume index (ESVI) at day 168 in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / LVEF (PPS) - Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Left ventricular ejection fraction (LVEF) at day 168 in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / EDVI (PPS) - Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
End diastolic volume index (EDVI) at day 168 in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / ESVI (PPS) - Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
End systolic volume index (ESVI) at day 168 in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / LVEF (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis
Subject analysis set description:	
Change in Left ventricular ejection fraction (LVEF) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).	
Subject analysis set title	BAY 1142524 / EDVI (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis
Subject analysis set description:	
Change in End diastolic volume index (EDVI) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).	
Subject analysis set title	BAY 1142524 / ESVI (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis
Subject analysis set description:	
Change in End systolic volume index (ESVI) from baseline to 6 months (Day 168) after treatment with BAY 1142524 in the full analysis set (FAS).	
Subject analysis set title	Placebo / LVEF (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis
Subject analysis set description:	
Change in Left ventricular ejection fraction (LVEF) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).	
Subject analysis set title	Placebo / EDVI (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Change in End diastolic volume index (EDVI) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).

Subject analysis set title	Placebo / ESVI (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Change in End systolic volume index (ESVI) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / LVEF (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at baseline in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / EDVI (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

End diastolic volume index (EDVI) at baseline in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / ESVI (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

End systolic volume index (ESVI) at baseline in the full analysis set (FAS).

Subject analysis set title	Placebo / LVEF (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at baseline in the full analysis set (FAS).

Subject analysis set title	Placebo / EDVI (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

End diastolic volume index (EDVI) at baseline in the full analysis set (FAS).

Subject analysis set title	Placebo / ESVI (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

End systolic volume index (ESVI) at baseline in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / LVEF (FAS) - Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at day 168 in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / EDVI (FAS) - Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

End diastolic volume index (EDVI) at day 168 in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / ESVI (FAS) - Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

End systolic volume index (ESVI) at day 168 in the full analysis set (FAS).

Subject analysis set title	Placebo / LVEF (FAS) - Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at day 168 in the full analysis set (FAS).

Subject analysis set title	Placebo / EDVI (FAS) - Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

End systolic volume index (ESVI) at day 168 in the full analysis set (FAS).

Subject analysis set title	Placebo / ESVI (FAS) - Day 168
Subject analysis set type	Full analysis
Subject analysis set description: End systolic volume index (ESVI) at day 168 in the full analysis set (FAS).	
Subject analysis set title	Per protocol analysis set (PPS) - BAY 1142524
Subject analysis set type	Per protocol
Subject analysis set description: Subjects valid for per protocol analysis	
Subject analysis set title	Per protocol analysis set (PPS) - Placebo
Subject analysis set type	Per protocol
Subject analysis set description: Subjects valid for per protocol analysis	
Subject analysis set title	Full analysis set (FAS) - BAY 1142524
Subject analysis set type	Full analysis
Subject analysis set description: Subjects valid for full analysis	
Subject analysis set title	Full analysis set (FAS) - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Subjects valid for full analysis	
Subject analysis set title	Safety analysis set (SAS) - BAY 1142524
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects valid for safety analysis	
Subject analysis set title	Safety analysis set (SAS)
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects valid for safety analysis	

Reporting group values	BAY 1142524 / LVEF (PPS) - Change: Baseline vs. Day 168	BAY 1142524 / EDVI (PPS) - Change: Baseline vs. Day 168	BAY 1142524 / ESVI (PPS) - Change: Baseline vs. Day 168
Number of subjects	42	42	42
Age Categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	35	35	35
From 65-84 years	7	7	7
85 years and over			
Gender Categorical Units: Subjects			
Female	4	4	4
Male	38	38	38

Reporting group values	Placebo / LVEF (PPS) - Change:	Placebo / EDVI (PPS) - Change: Baseline	Placebo / ESVI (PPS) - Change: Baseline

	Baseline vs. Day 168	vs. Day 168	vs. Day 168
Number of subjects	38	38	38
Age Categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	33	33	33
From 65-84 years	5	5	5
85 years and over			
Gender Categorical			
Units: Subjects			
Female	8	8	8
Male	30	30	30

Reporting group values	BAY 1142524 / LVEF (PPS) - Baseline	BAY 1142524 / EDVI (PPS) - Baseline	BAY 1142524 / ESVI (PPS) - Baseline
Number of subjects	42	42	42
Age Categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	35	35	35
From 65-84 years	7	7	7
85 years and over			
Gender Categorical			
Units: Subjects			
Female	4	4	4
Male	38	38	38

Reporting group values	Placebo / LVEF (PPS) - Baseline	Placebo / EDVI (PPS) - Baseline	Placebo / ESVI (PPS) - Baseline
Number of subjects	38	38	38
Age Categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			

Adults (18-64 years)	33	33	33
From 65-84 years	5	5	5
85 years and over			
Gender Categorical			
Units: Subjects			
Female	8	8	8
Male	30	30	30

Reporting group values	BAY 1142524 / LVEF (PPS) - Day 168	BAY 1142524 / EDVI (PPS) - Day 168	BAY 1142524 / ESVI (PPS) - Day 168
Number of subjects	42	42	42
Age Categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	35	35	35
From 65-84 years	7	7	7
85 years and over			
Gender Categorical			
Units: Subjects			
Female	4	4	4
Male	38	38	38

Reporting group values	Placebo / LVEF (PPS) - Day 168	Placebo / EDVI (PPS) - Day 168	Placebo / ESVI (PPS) - Day 168
Number of subjects	38	38	38
Age Categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	33	33	33
From 65-84 years	5	5	5
85 years and over			
Gender Categorical			
Units: Subjects			
Female	8	8	8
Male	30	30	30

Reporting group values	BAY 1142524 / LVEF (FAS) - Change: Baseline vs. Day 168	BAY 1142524 / EDVI (FAS) - Change: Baseline vs. Day 168	BAY 1142524 / ESVI (FAS) - Change: Baseline vs. Day 168
Number of subjects	54	54	54

Age Categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	45	45	45
From 65-84 years	9	9	9
85 years and over			
Gender Categorical Units: Subjects			
Female	5	5	5
Male	49	49	49

Reporting group values	Placebo / LVEF (FAS) - Change: Baseline vs. Day 168	Placebo / EDVI (FAS) - Change: Baseline vs. Day 168	Placebo / ESVI (FAS) - Change: Baseline vs. Day 168
Number of subjects	53	53	53
Age Categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	44	44	44
From 65-84 years	9	9	9
85 years and over			
Gender Categorical Units: Subjects			
Female	9	9	9
Male	44	44	44

Reporting group values	BAY 1142524 / LVEF (FAS) - Baseline	BAY 1142524 / EDVI (FAS) - Baseline	BAY 1142524 / ESVI (FAS) - Baseline
Number of subjects	54	54	54
Age Categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	45	45	45

From 65-84 years	9	9	9
85 years and over			

Gender Categorical			
Units: Subjects			
Female	5	5	5
Male	49	49	49

Reporting group values	Placebo / LVEF (FAS) - Baseline	Placebo / EDVI (FAS) - Baseline	Placebo / ESVI (FAS) - Baseline
Number of subjects	53	53	53
Age Categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	44	44	44
From 65-84 years	9	9	9
85 years and over			
Gender Categorical			
Units: Subjects			
Female	9	9	9
Male	44	44	44

Reporting group values	BAY 1142524 / LVEF (FAS) - Day 168	BAY 1142524 / EDVI (FAS) - Day 168	BAY 1142524 / ESVI (FAS) - Day 168
Number of subjects	54	54	54
Age Categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	45	45	45
From 65-84 years	9	9	9
85 years and over			
Gender Categorical			
Units: Subjects			
Female	5	5	5
Male	49	49	49

Reporting group values	Placebo / LVEF (FAS) - Day 168	Placebo / EDVI (FAS) - Day 168	Placebo / ESVI (FAS) - Day 168
Number of subjects	53	53	53

Age Categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	44	44	44
From 65-84 years	9	9	9
85 years and over			
Gender Categorical Units: Subjects			
Female	9	9	9
Male	44	44	44

Reporting group values	Per protocol analysis set (PPS) - BAY 1142524	Per protocol analysis set (PPS) - Placebo	Full analysis set (FAS) - BAY 1142524
Number of subjects	42	38	54
Age Categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	35	33	45
From 65-84 years	7	5	9
85 years and over			
Gender Categorical Units: Subjects			
Female	4	8	5
Male	38	30	49

Reporting group values	Full analysis set (FAS) - Placebo	Safety analysis set (SAS) - BAY 1142524	Safety analysis set (SAS)
Number of subjects	53	54	107
Age Categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	44	45	44

From 65-84 years 85 years and over	9	9	9

Gender Categorical Units: Subjects			
Female	9	5	9
Male	44	49	44

End points

End points reporting groups

Reporting group title	BAY 1142524
Reporting group description:	
Efficacy evaluation was performed in the per protocol set (PPS) and full analysis set (FAS). A total of 42 subjects in the BAY 1142524 arm were valid for the PPS and 54 subjects for the FAS.	
Reporting group title	Placebo
Reporting group description:	
Efficacy evaluation was performed in the per protocol set (PPS) and full analysis set (FAS). A total of 38 subjects in the placebo arm were valid for the PPS and 53 subjects for the FAS.	
Subject analysis set title	BAY 1142524 / LVEF (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in Left ventricular ejection fraction (LVEF) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / EDVI (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in End diastolic volume index (EDVI) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / ESVI (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in End systolic volume index (ESVI) from baseline to 6 months (Day 168) after treatment with BAY 1142524 in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / LVEF (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in Left ventricular ejection fraction (LVEF) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / EDVI (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in End diastolic volume index (EDVI) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	Placebo / ESVI (PPS) - Change: Baseline vs. Day 168
Subject analysis set type	Per protocol
Subject analysis set description:	
Change in End systolic volume index (ESVI) from baseline to 6 months (Day 168) after treatment with Placebo in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / LVEF (PPS) - Baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
Left ventricular ejection fraction (LVEF) at baseline in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / EDVI (PPS) - Baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
End diastolic volume index (EDVI) at baseline in the protocol analysis set (PPS).	
Subject analysis set title	BAY 1142524 / ESVI (PPS) - Baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
End systolic volume index (ESVI) at baseline in the protocol analysis set (PPS).	

Subject analysis set title	Placebo / LVEF (PPS) - Baseline
Subject analysis set type	Per protocol

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at baseline in the protocol analysis set (PPS).

Subject analysis set title	Placebo / EDVI (PPS) - Baseline
Subject analysis set type	Per protocol

Subject analysis set description:

End diastolic volume index (EDVI) at baseline in the protocol analysis set (PPS).

Subject analysis set title	Placebo / ESVI (PPS) - Baseline
Subject analysis set type	Per protocol

Subject analysis set description:

End systolic volume index (ESVI) at baseline in the protocol analysis set (PPS).

Subject analysis set title	BAY 1142524 / LVEF (PPS) - Day 168
Subject analysis set type	Per protocol

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at day 168 in the protocol analysis set (PPS).

Subject analysis set title	BAY 1142524 / EDVI (PPS) - Day 168
Subject analysis set type	Per protocol

Subject analysis set description:

End diastolic volume index (EDVI) at day 168 in the protocol analysis set (PPS).

Subject analysis set title	BAY 1142524 / ESVI (PPS) - Day 168
Subject analysis set type	Per protocol

Subject analysis set description:

End systolic volume index (ESVI) at day 168 in the protocol analysis set (PPS).

Subject analysis set title	Placebo / LVEF (PPS) - Day 168
Subject analysis set type	Per protocol

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at day 168 in the protocol analysis set (PPS).

Subject analysis set title	Placebo / EDVI (PPS) - Day 168
Subject analysis set type	Per protocol

Subject analysis set description:

End diastolic volume index (EDVI) at day 168 in the protocol analysis set (PPS).

Subject analysis set title	Placebo / ESVI (PPS) - Day 168
Subject analysis set type	Per protocol

Subject analysis set description:

End systolic volume index (ESVI) at day 168 in the protocol analysis set (PPS).

Subject analysis set title	BAY 1142524 / LVEF (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Change in Left ventricular ejection fraction (LVEF) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / EDVI (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Change in End diastolic volume index (EDVI) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / ESVI (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Change in End systolic volume index (ESVI) from baseline to 6 months (Day 168) after treatment with BAY 1142524 in the full analysis set (FAS).

Subject analysis set title	Placebo / LVEF (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Change in Left ventricular ejection fraction (LVEF) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).

Subject analysis set title	Placebo / EDVI (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Change in End diastolic volume index (EDVI) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).

Subject analysis set title	Placebo / ESVI (FAS) - Change: Baseline vs. Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Change in End systolic volume index (ESVI) from baseline to 6 months (Day 168) after treatment with Placebo in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / LVEF (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at baseline in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / EDVI (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

End diastolic volume index (EDVI) at baseline in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / ESVI (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

End systolic volume index (ESVI) at baseline in the full analysis set (FAS).

Subject analysis set title	Placebo / LVEF (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at baseline in the full analysis set (FAS).

Subject analysis set title	Placebo / EDVI (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

End diastolic volume index (EDVI) at baseline in the full analysis set (FAS).

Subject analysis set title	Placebo / ESVI (FAS) - Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

End systolic volume index (ESVI) at baseline in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / LVEF (FAS) - Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at day 168 in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / EDVI (FAS) - Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

End diastolic volume index (EDVI) at day 168 in the full analysis set (FAS).

Subject analysis set title	BAY 1142524 / ESVI (FAS) - Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

End systolic volume index (ESVI) at day 168 in the full analysis set (FAS).

Subject analysis set title	Placebo / LVEF (FAS) - Day 168
Subject analysis set type	Full analysis

Subject analysis set description:

Left ventricular ejection fraction (LVEF) at day 168 in the full analysis set (FAS).

Subject analysis set title	Placebo / EDVI (FAS) - Day 168
Subject analysis set type	Full analysis
Subject analysis set description: End systolic volume index (ESVI) at day 168 in the full analysis set (FAS).	
Subject analysis set title	Placebo / ESVI (FAS) - Day 168
Subject analysis set type	Full analysis
Subject analysis set description: End systolic volume index (ESVI) at day 168 in the full analysis set (FAS).	
Subject analysis set title	Per protocol analysis set (PPS) - BAY 1142524
Subject analysis set type	Per protocol
Subject analysis set description: Subjects valid for per protocol analysis	
Subject analysis set title	Per protocol analysis set (PPS) - Placebo
Subject analysis set type	Per protocol
Subject analysis set description: Subjects valid for per protocol analysis	
Subject analysis set title	Full analysis set (FAS) - BAY 1142524
Subject analysis set type	Full analysis
Subject analysis set description: Subjects valid for full analysis	
Subject analysis set title	Full analysis set (FAS) - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Subjects valid for full analysis	
Subject analysis set title	Safety analysis set (SAS) - BAY 1142524
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects valid for safety analysis	
Subject analysis set title	Safety analysis set (SAS)
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects valid for safety analysis	

Primary: LVEF (%) - PPS

End point title	LVEF (%) - PPS
End point description:	
End point type	Primary
End point timeframe: Baseline vs. Day 168	

End point values	BAY 1142524 / LVEF (PPS) - Change: Baseline vs. Day 168	Placebo / LVEF (PPS) - Change: Baseline vs. Day 168	BAY 1142524 / LVEF (PPS) - Baseline	Placebo / LVEF (PPS) - Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[1]	38[2]	42[3]	38[4]
Units: percent				
arithmetic mean (full range (min-max))	3.51 (-7.3 to	3.97 (-5.4 to	39.08 (24.3 to	37.18 (28.0 to

	16.2)	16.7)	48.0)	46.6)

Notes:

[1] - Left ventricular ejection fraction (LVEF)

[2] - Left ventricular ejection fraction (LVEF)

[3] - Left ventricular ejection fraction (LVEF)

[4] - Left ventricular ejection fraction (LVEF)

End point values	BAY 1142524 / LVEF (PPS) - Day 168	Placebo / LVEF (PPS) - Day 168		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	42[5]	38[6]		
Units: percent				
arithmetic mean (full range (min-max))	42.59 (24.4 to 59.7)	41.15 (25.8 to 55.4)		

Notes:

[5] - Left ventricular ejection fraction (LVEF)

[6] - Left ventricular ejection fraction (LVEF)

Statistical analyses

Statistical analysis title	LVEF (%)
Comparison groups	BAY 1142524 / LVEF (PPS) - Change: Baseline vs. Day 168 v Placebo / LVEF (PPS) - Change: Baseline vs. Day 168
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-0.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.39
upper limit	1.47

Statistical analysis title	LVEF (%)
Comparison groups	BAY 1142524 / LVEF (PPS) - Baseline v Placebo / LVEF (PPS) - Baseline
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	1.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.25
upper limit	4.05

Statistical analysis title	LVEF (%)
Comparison groups	BAY 1142524 / LVEF (PPS) - Day 168 v Placebo / LVEF (PPS) - Day 168
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	1.44
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.69
upper limit	4.56

Primary: EDVI (mL/m2) - PPS	
End point title	EDVI (mL/m2) - PPS
End point description: End diastolic volume index (EDVI)	
End point type	Primary
End point timeframe: Baseline vs. Day 168	

End point values	BAY 1142524 / EDVI (PPS) - Change: Baseline vs. Day 168	Placebo / EDVI (PPS) - Change: Baseline vs. Day 168	BAY 1142524 / EDVI (PPS) - Baseline	Placebo / EDVI (PPS) - Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[7]	38[8]	42[9]	38[10]
Units: mL/m2				
arithmetic mean (full range (min-max))	7.32 (-22.7 to 37.6)	5.07 (-39.5 to 52.1)	77.38 (44.7 to 154.6)	80.02 (53.1 to 109.3)

Notes:

[7] - End diastolic volume index (EDVI)

[8] - End diastolic volume index (EDVI)

[9] - End diastolic volume index (EDVI)

[10] - End diastolic volume index (EDVI)

End point values	BAY 1142524 / EDVI (PPS) - Day 168	Placebo / EDVI (PPS) - Day 168		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	42[11]	38[12]		
Units: mL/m2				

arithmetic mean (full range (min-max))	84.7 (44.4 to 175.5)	85.09 (43.6 to 123.7)		

Notes:

[11] - End diastolic volume index (EDVI)

[12] - End diastolic volume index (EDVI)

Statistical analyses

Statistical analysis title	EDVI (mL/m2)
Comparison groups	BAY 1142524 / EDVI (PPS) - Change: Baseline vs. Day 168 v Placebo / EDVI (PPS) - Change: Baseline vs. Day 168
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	2.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.78
upper limit	8.28

Statistical analysis title	EDVI (mL/m2)
Comparison groups	BAY 1142524 / EDVI (PPS) - Baseline v Placebo / EDVI (PPS) - Baseline
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-2.64
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.24
upper limit	3.96

Statistical analysis title	EDVI (mL/m2)
Comparison groups	BAY 1142524 / EDVI (PPS) - Day 168 v Placebo / EDVI (PPS) - Day 168

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-0.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.4
upper limit	7.62

Primary: ESVI (mL/m2) - PPS	
End point title	ESVI (mL/m2) - PPS
End point description: End systolic volume index (ESVI)	
End point type	Primary
End point timeframe: Baseline vs. Day 168	

End point values	BAY 1142524 / ESVI (PPS) - Change: Baseline vs. Day 168	Placebo / ESVI (PPS) - Change: Baseline vs. Day 168	BAY 1142524 / ESVI (PPS) - Baseline	Placebo / ESVI (PPS) - Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[13]	38[14]	42[15]	38[16]
Units: mL/m2				
arithmetic mean (full range (min-max))	2.29 (-22.8 to 30.2)	0.57 (-27.8 to 41.9)	47.33 (26.0 to 89.0)	50.52 (29.2 to 75.5)

Notes:

[13] - End systolic volume index (ESVI)

[14] - End systolic volume index (ESVI)

[15] - End systolic volume index (ESVI)

[16] - End systolic volume index (ESVI)

End point values	BAY 1142524 / ESVI (PPS) - Day 168	Placebo / ESVI (PPS) - Day 168		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	42[17]	38[18]		
Units: mL/m2				
arithmetic mean (full range (min-max))	49.62 (20.5 to 101.9)	51.09 (19.5 to 82.6)		

Notes:

[17] - End systolic volume index (ESVI)

[18] - End systolic volume index (ESVI)

Statistical analyses

Statistical analysis title	ESVI (mL/m2)
Comparison groups	BAY 1142524 / ESVI (PPS) - Change: Baseline vs. Day 168 v Placebo / ESVI (PPS) - Change: Baseline vs. Day 168
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	1.72
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.14
upper limit	6.58

Statistical analysis title	ESVI (mL/m2)
Comparison groups	BAY 1142524 / ESVI (PPS) - Baseline v Placebo / ESVI (PPS) - Baseline
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-3.19
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.89
upper limit	1.51

Statistical analysis title	ESVI (mL/m2)
Comparison groups	BAY 1142524 / ESVI (PPS) - Day 168 v Placebo / ESVI (PPS) - Day 168
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-1.47
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.01
upper limit	5.07

Primary: LVEF (%) - FAS

End point title	LVEF (%) - FAS
End point description: Left ventricular ejection fraction (LVEF)	
End point type	Primary
End point timeframe: Baseline vs. Day 168	

End point values	BAY 1142524 / LVEF (FAS) - Change: Baseline vs. Day 168	Placebo / LVEF (FAS) - Change: Baseline vs. Day 168	BAY 1142524 / LVEF (FAS) - Baseline	Placebo / LVEF (FAS) - Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	47[19]	48[20]	47[21]	48[22]
Units: percent				
arithmetic mean (full range (min-max))	3.67 (-7.3 to 16.2)	4.00 (-5.4 to 16.7)	39.13 (24.3 to 48.0)	37.0 (22.9 to 46.6)

Notes:

[19] - Left ventricular ejection fraction (LVEF)

[20] - Left ventricular ejection fraction (LVEF)

[21] - Left ventricular ejection fraction (LVEF)

[22] - Left ventricular ejection fraction (LVEF)

End point values	BAY 1142524 / LVEF (FAS) - Day 168	Placebo / LVEF (FAS) - Day 168		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	47[23]	48[24]		
Units: percent				
arithmetic mean (full range (min-max))	42.8 (24.4 to 59.7)	41.0 (21.7 to 55.4)		

Notes:

[23] - Left ventricular ejection fraction (LVEF)

[24] - Left ventricular ejection fraction (LVEF)

Statistical analyses

Statistical analysis title	LVEF (%)
Comparison groups	BAY 1142524 / LVEF (FAS) - Change: Baseline vs. Day 168 v Placebo / LVEF (FAS) - Change: Baseline vs. Day 168
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-0.33

Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.04
upper limit	1.38

Statistical analysis title	LVEF (%)
Comparison groups	BAY 1142524 / LVEF (FAS) - Baseline v Placebo / LVEF (FAS) - Baseline
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	2.13
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.15
upper limit	4.12

Statistical analysis title	LVEF (%)
Comparison groups	BAY 1142524 / LVEF (FAS) - Day 168 v Placebo / LVEF (FAS) - Day 168
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	1.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.03
upper limit	4.64

Primary: EDVI (mL/m2) - FAS	
End point title	EDVI (mL/m2) - FAS
End point description: End diastolic volume index (EDVI)	
End point type	Primary
End point timeframe: Baseline vs. Day 168	

End point values	BAY 1142524 / EDVI (FAS) - Change: Baseline vs. Day 168	Placebo / EDVI (FAS) - Change: Baseline vs. Day 168	BAY 1142524 / EDVI (FAS) - Baseline	Placebo / EDVI (FAS) - Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	47[25]	48[26]	47[27]	48[28]
Units: mL/m2				
arithmetic mean (full range (min-max))	6.89 (-22.7 to 37.6)	6.11 (-39.5 to 66.8)	75.53 (44.7 to 154.6)	79.24 (53.1 to 117.1)

Notes:

[25] - End diastolic volume index (EDVI)

[26] - End diastolic volume index (EDVI)

[27] - End diastolic volume index (EDVI)

[28] - End diastolic volume index (EDVI)

End point values	BAY 1142524 / EDVI (FAS) - Day 168	Placebo / EDVI (FAS) - Day 168		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	47[29]	48[30]		
Units: mL/m2				
arithmetic mean (full range (min-max))	82.42 (44.0 to 175.5)	85.35 (43.6 to 132.6)		

Notes:

[29] - End diastolic volume index (EDVI)

[30] - End diastolic volume index (EDVI)

Statistical analyses

Statistical analysis title	EDVI (mL/m2)
Comparison groups	BAY 1142524 / EDVI (FAS) - Change: Baseline vs. Day 168 v Placebo / EDVI (FAS) - Change: Baseline vs. Day 168
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	0.78
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.01
upper limit	6.57

Statistical analysis title	EDVI (mL/m2)
Comparison groups	BAY 1142524 / EDVI (FAS) - Day 168 v Placebo / EDVI (FAS) - Day 168

Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-2.93
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.42
upper limit	4.56

Statistical analysis title	EDVI (mL/m2)
Comparison groups	BAY 1142524 / EDVI (FAS) - Baseline v Placebo / EDVI (FAS) - Baseline
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-3.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.82
upper limit	2.4

Primary: ESVI (mL/m2) - FAS	
End point title	ESVI (mL/m2) - FAS
End point description: End systolic volume index (ESVI)	
End point type	Primary
End point timeframe: Baseline vs. Day 168	

End point values	BAY 1142524 / ESVI (FAS) - Change: Baseline vs. Day 168	Placebo / ESVI (FAS) - Change: Baseline vs. Day 168	BAY 1142524 / ESVI (FAS) - Baseline	Placebo / ESVI (FAS) - Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	47[31]	48[32]	47[33]	48[34]
Units: mL/m2				
arithmetic mean (full range (min-max))	1.89 (-22.8 to 30.2)	1.35 (-27.8 to 53.2)	46.14 (26.0 to 89.0)	50.09 (29.2 to 82.3)

Notes:
[31] - End systolic volume index (ESVI)
[32] - End systolic volume index (ESVI)
[33] - End systolic volume index (ESVI)
[34] - End systolic volume index (ESVI)

End point values	BAY 1142524 / ESVI (FAS) - Day 168	Placebo / ESVI (FAS) - Day 168		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	47[35]	48[36]		
Units: mL/m2				
arithmetic mean (full range (min-max))	48.03 (20.5 to 101.9)	51.45 (19.5 to 102.3)		

Notes:
[35] - End systolic volume index (ESVI)
[36] - End systolic volume index (ESVI)

Statistical analyses

Statistical analysis title	ESVI (mL/m2)
Comparison groups	BAY 1142524 / ESVI (FAS) - Change: Baseline vs. Day 168 v Placebo / ESVI (FAS) - Change: Baseline vs. Day 168
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	0.54
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.12
upper limit	5.19

Statistical analysis title	ESVI (mL/m2)
Comparison groups	BAY 1142524 / ESVI (FAS) - Baseline v Placebo / ESVI (FAS) - Baseline
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-3.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.26
upper limit	0.35

Statistical analysis title	ESVI (mL/m2)
Comparison groups	BAY 1142524 / ESVI (FAS) - Day 168 v Placebo / ESVI (FAS) - Day 168
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	-3.42
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.57
upper limit	2.73

Secondary: Number of TEAEs

End point title	Number of TEAEs

End point description:

Treatment emergent adverse event (TEAE): TEAEs were defined as AEs occurring after the start of study drug but no more than 7 days after the stop of study drug.

End point type	Secondary

End point timeframe:

From the first study drug administration until 7 days after the stop of study

End point values	BAY 1142524	Placebo	Safety analysis set (SAS)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	54	53	107	
Units: Subjects	35	40	75	

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of TEAEs: Mild

End point title	Severity of TEAEs: Mild

End point description:

Treatment emergent adverse event (TEAE): TEAEs were defined as AEs occurring after the start of study drug but no more than 7 days after the stop of study drug.

End point type	Secondary

End point timeframe:

From the first study drug administration until 7 days after the stop of study

End point values	BAY 1142524	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: Subjects	21	23		

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of TEAEs: Moderate

End point title	Severity of TEAEs: Moderate

End point description:

Treatment emergent adverse event (TEAE): TEAEs were defined as AEs occurring after the start of study drug but no more than 7 days after the stop of study drug.

End point type	Secondary

End point timeframe:

From the first study drug administration until 7 days after the stop of study

End point values	BAY 1142524	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: Subjects	11	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of TEAEs: Severe

End point title	Severity of TEAEs: Severe

End point description:

Treatment emergent adverse event (TEAE): TEAEs were defined as AEs occurring after the start of study drug but no more than 7 days after the stop of study drug.

End point type	Secondary

End point timeframe:

From the first study drug administration until 7 days after the stop of study

End point values	BAY 1142524	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: Subjects	3	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
After the start of study drug but no more than 7 days after the stop of study drug.	
Adverse event reporting additional description:	
All 107 subjects who received the study drug were included in the safety analysis set.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	BAY 1142524
Reporting group description:	
A total of 42 subjects in the BAY 1142524 arm were valid for the PPS and 54 subjects for the FAS.	
Reporting group title	Placebo
Reporting group description:	
A total of 38 subjects in the placebo arm were valid for the PPS and 53 subjects for the FAS.	

Serious adverse events	BAY 1142524	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 54 (20.37%)	9 / 53 (16.98%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tonsil cancer			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			

subjects affected / exposed	2 / 54 (3.70%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular dysfunction			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (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			
Angioplasty			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
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	1 / 54 (1.85%)	0 / 53 (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			
Chest pain			
subjects affected / exposed	3 / 54 (5.56%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (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			
Dyspnoea			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (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	BAY 1142524	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 54 (62.96%)	40 / 53 (75.47%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oral fibroma			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 54 (0.00%)	2 / 53 (3.77%)	
occurrences (all)	0	2	
Hypotension			
subjects affected / exposed	6 / 54 (11.11%)	3 / 53 (5.66%)	
occurrences (all)	10	4	
Peripheral vascular disorder			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Raynaud's phenomenon			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Hot flush			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Bunion operation			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 54 (5.56%)	3 / 53 (5.66%)	
occurrences (all)	4	3	
Chest pain			
subjects affected / exposed	6 / 54 (11.11%)	8 / 53 (15.09%)	
occurrences (all)	7	9	
Fatigue			

subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Gait disturbance			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Hyperthermia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	1 / 54 (1.85%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
Peripheral swelling			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Exercise tolerance decreased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Nipple pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Vaginal haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 54 (3.70%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Dyspnoea			
subjects affected / exposed	2 / 54 (3.70%)	4 / 53 (7.55%)	
occurrences (all)	2	5	
Dyspnoea exertional			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	2 / 54 (3.70%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
Epistaxis			
subjects affected / exposed	1 / 54 (1.85%)	2 / 53 (3.77%)	
occurrences (all)	1	3	
Haemoptysis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal discomfort			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anger			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	2	
Depressed mood			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Insomnia			

subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Stress			
subjects affected / exposed	0 / 54 (0.00%)	2 / 53 (3.77%)	
occurrences (all)	0	2	
Somatic symptom disorder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 54 (1.85%)	3 / 53 (5.66%)	
occurrences (all)	1	4	
Blood potassium increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Blood triglycerides increased			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Weight increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Hepatic enzyme increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Pancreatic enzymes increased			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Liver function test increased			

subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Head injury			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Face injury			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Joint injury			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Bradycardia			
subjects affected / exposed	1 / 54 (1.85%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
Cardiac failure congestive			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Coronary artery stenosis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Palpitations			

subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Cardiac ventricular thrombosis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 54 (7.41%)	0 / 53 (0.00%)	
occurrences (all)	4	0	
Headache			
subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Hypoaesthesia			
subjects affected / exposed	1 / 54 (1.85%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
Syncope			
subjects affected / exposed	2 / 54 (3.70%)	1 / 53 (1.89%)	
occurrences (all)	2	1	
Orthostatic intolerance			
subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Leukopenia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Pancytopenia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	2	
Abdominal pain			
subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Abdominal pain lower			
subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	2 / 54 (3.70%)	1 / 53 (1.89%)	
occurrences (all)	2	1	
Chronic gastritis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	2 / 54 (3.70%)	1 / 53 (1.89%)	
occurrences (all)	2	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Gingival bleeding			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Nausea			

subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Pancreatitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Erosive duodenitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Faeces soft			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Noninfective gingivitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Skin irritation			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Umbilical haematoma			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			

subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Renal cyst			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Strangury			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	2 / 54 (3.70%)	1 / 53 (1.89%)	
occurrences (all)	2	1	
Muscle spasms			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	4 / 54 (7.41%)	1 / 53 (1.89%)	
occurrences (all)	4	1	
Myopathy			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Polymyalgia rheumatica			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Limb discomfort			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Infections and infestations			

Cystitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	2 / 54 (3.70%)	3 / 53 (5.66%)	
occurrences (all)	2	3	
Pneumonia			
subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Urinary tract infection			
subjects affected / exposed	1 / 54 (1.85%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
Infected dermal cyst			
subjects affected / exposed	1 / 54 (1.85%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Candida infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	2 / 54 (3.70%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
Folate deficiency			
subjects affected / exposed	0 / 54 (0.00%)	1 / 53 (1.89%)	
occurrences (all)	0	1	
Glucose tolerance impaired			
subjects affected / exposed	1 / 54 (1.85%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Hyperkalaemia			

subjects affected / exposed occurrences (all)	2 / 54 (3.70%) 2	1 / 53 (1.89%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 October 2016	Amendment 1, Version 2.0, dated 14 OCT 2016, was globally implemented in order to consider the comments and feedbacks from German authority Bundesinstitut für Arzneimittel und Medizinprodukte: - Inclusion of only clinically stable patients after MI and not subjects with MI in an emergency situation. - It was clarified that the assignment of subjects to analysis sets was made during the Validity Review Meeting and documented in the Validity Review Report. Subjects were analyzed according to their actual treatment. - It was clarified that the statistical test was to be performed using a one sided alpha level. - A withdrawal criterion was added regarding subjects suffering from relevant symptomatic hypotension. - The determination of End of Study was modified to be LPLV as requested by the BfArM. - It was clarified which situations required an obligatory termination of the study and which situations required an optional termination of the study by the sponsor. - Physical examination was added in all visits during the treatment to ensure detection of early signs of cardiac decompensation. - Re-screening was deleted in the withdrawal section as this was allowed in this study. - Withdrawal criteria were modified to include information that subjects who required cardiac device implantation during the study had to be withdrawn from the study.
03 November 2016	Amendment 2, Version 3.0, dated 03 NOV 2016, was globally implemented in order to consider the comments and feedbacks from the Czech Republic (State Institute for Drug Control) and the German BfArM: - An additional visit (14 ± 4 days after first study drug intake) was introduced to improve adherence of the subjects to the study protocol and to check drug accountability. - Premature termination of the study was modified based upon the request by the BfArM.
15 May 2017	Amendment 3, Version 4.0, dated 15 MAY 2017, was globally implemented in order to consider feedback from the investigational sites: - Leukocytes and erythrocytes were added for urinalysis parameters. - It was clarified that the breakfast and concomitant medication could be taken at home in the morning of visit 1 in case the subject was not hospitalized anymore. - It was clarified that the blood sample for laboratory safety parameters had to be measured before first study drug administration, but the results were not necessarily required before first study drug administration.
24 October 2017	Amendment 4, Version 5.0, 24 OCT 2017, was globally implemented as the observed dropout/invalidity rate was higher than originally anticipated: - The number of randomized and enrolled subjects was increased in order to reach the target of 60 valid subjects (30 valid completers per treatment arm)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As exploratory outcomes were analyzed: cardiovascular hospitalization mortality, re-hospitalization for heart failure, cardiovascular hospitalization rate, infarct size, wall motility score index, pharmacokinetics and biomarkers

Notes: