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Trial record **1 of 1** for: CLCZ696B2214

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LCZ696 Compared to Valsartan in Patients With Chronic Heart Failure and Preserved Left-ventricular Ejection Fraction

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00887588

First received: April 22, 2009
Last updated: August 12, 2015
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History of Changes

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Results First Received: July 16, 2015

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Chronic Heart Failure
Interventions:	Drug: LCZ696 Drug: Valsartan Drug: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
A total of 308 participants were randomized to the core 12 week period, but 7 participants were excluded due to major Good Clinical Practice (GCP) violation. Of the 261 participants who completed the core, 252 participants entered the extension period.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Eight participants, who completed the core, could not continue in the extension because the 36 week protocol amendment was not yet approved by health authorities; 1 participant, who completed the core, discontinued before the extension start due to an adverse event.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Participant Flow for 2 periods

Period 1: Core Period

	LCZ696	Valsartan
STARTED	**149**	**152**
Extension Efficacy Set	**127**	**125**

Full Analysis Set	**148**	**146**
Arterial Stiffness Set	**86**	**94**
COMPLETED	**130**	**131**
NOT COMPLETED	**19**	**21**
Death	**1**	**1**
Lost to Follow-up	**3**	**1**
Withdrawal by Subject	**6**	**8**
Adverse Event	**9**	**11**

Period 2: Extension Period

	LCZ696	Valsartan
STARTED	**127**	**125**
Arterial Stiffness Set	**86**	**94**
COMPLETED	**121**	**120**
NOT COMPLETED	**6**	**5**
Adverse Event	**4**	**4**
Death	**0**	**1**
Protocol deviation	**1**	**0**
Lost to Follow-up	**1**	**0**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.
Total	Total of all reporting groups

Baseline Measures

	LCZ696	Valsartan	Total
Number of Participants [units: participants]	**149**	**152**	**301**
Age [units: Years] Mean (Standard Deviation)	**70.9 (9.38)**	**71.2 (8.94)**	**71.0 (9.15)**
Gender [units: Participants]			
Female	**85**	**85**	**170**
Male	**64**	**67**	**131**

Outcome Measures

Hide All Outcome Measures

1. Primary: Change From Baseline in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP) [Time Frame: Baseline, 12 weeks]

Measure Type	Primary
Measure Title	Change From Baseline in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP)
Measure Description	Evaluation of NT-proBNP was performed by a central laboratory. Change from baseline in NT-proBNP was presented as a ratio where the ratio was calculated as the NT-proBNP value at 12 weeks over the NT-proBNP value at baseline. A ratio < 1 indicates improvement.
Time Frame	Baseline, 12 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the full analysis set (FAS), who had both baseline and 12 week values, were included in the analysis. The FAS consisted of all randomized participants who had baseline and at least one post-baseline efficacy measurement during the double blind period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	**Valsartan**

Number of Participants Analyzed [units: participants]	**134**	**132**
Change From Baseline in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP) [units: ratio: endpoint/baseline (pg/mL)] Geometric Mean (95% Confidence Interval)	**0.83 (0.68 to 1.01)**	**1.08 (0.89 to 1.32)**

No statistical analysis provided for Change From Baseline in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP)

2. Secondary: Change From Baseline in NT-proBNP and Brain Natriuretic Peptide (BNP) [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in NT-proBNP and Brain Natriuretic Peptide (BNP)
Measure Description	Evaluation of NT-proBNP and BNP was performed by a central laboratory. Change from baseline in NT-proBNP and in BNP was presented as a ratio where the ratio for NT-proBNP was calculated as the NT-proBNP value at 36 weeks over the NT-proBNP value at baseline, and the ratio for BNP was calculated as the BNP value at 36 weeks over the BNP value at baseline. A ratio < 1 indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values for each parameter, were included in the analysis for that parameter. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description

LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	**Valsartan**
Number of Participants Analyzed [units: participants]	**127**	**125**
Change From Baseline in NT-proBNP and Brain Natriuretic Peptide (BNP) [units: ratio: endpoint/baseline (pg/mL)] Geometric Mean (95% Confidence Interval)		
NT-proBNP (n=115,116)	**0.78 (0.59 to 1.02)**	**0.92 (0.70 to 1.21)**
BNP (n=116,113)	**1.14 (0.88 to 1.47)**	**0.95 (0.73 to 1.23)**

No statistical analysis provided for Change From Baseline in NT-proBNP and Brain Natriuretic Peptide (BNP)

3. Secondary: Change From Baseline in Plasma Cyclic Guanine Monophosphate (cGMP) [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Plasma Cyclic Guanine Monophosphate (cGMP)
Measure Description	Evaluation of cGMP was performed by a central laboratory. Change from baseline in cGMP was presented as a ratio where the ratio was calculated as the cGMP value at 36 weeks over the cGMP value at baseline. A ratio < 1 indicates improvement.

Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values, were included in the analysis for that parameter. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**56**	**54**
Change From Baseline in Plasma Cyclic Guanine Monophosphate (cGMP) [units: ratio: endpoint/baseline (nmol/L)] Geometric Mean (95% Confidence Interval)	**0.90 (0.78 to 1.03)**	**0.85 (0.73 to 0.99)**

No statistical analysis provided for Change From Baseline in Plasma Cyclic Guanine Monophosphate (cGMP)

4. Secondary: Change From Baseline in Echocardiography (ECHO) Parameters: Left Ventricular End (LVE) Diastolic Diameter, LVE Systolic Diameter, Septal End Diastolic Thickness, Posterior LV Wall End Diastolic Thickness, Relative Wall Thickness, Left Atrial Dimension [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Echocardiography (ECHO) Parameters: Left Ventricular End (LVE) Diastolic Diameter, LVE Systolic Diameter, Septal End Diastolic Thickness, Posterior LV Wall End Diastolic Thickness, Relative Wall Thickness, Left Atrial Dimension
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A negative change from baseline indicates improvement.
Time Frame	Baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values for each parameter, were included in the analysis for that parameter. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**127**	**125**
Change From Baseline in Echocardiography (ECHO) Parameters: Left Ventricular End (LVE) Diastolic Diameter, LVE Systolic Diameter, Septal End Diastolic Thickness, Posterior LV Wall End Diastolic Thickness, Relative Wall Thickness, Left Atrial Dimension [units: cm] Least Squares Mean (Standard Error)		
LVE diastolic diameter (n=98,107)	**-0.23 (0.051)**	**-0.19 (0.051)**
LVE systolic diameter (n=98,107)	**-0.12 (0.044)**	**-0.11 (0.044)**
Septal end diastolic thickness (n=98,106)	**0.01 (0.020)**	**0.01 (0.020)**
Post. LV wall end diastolic thickness (n=99,107)	**0.00 (0.015)**	**0.01 (0.015)**
Relative wall thickness (n=98,107)	**0.02 (0.008)**	**0.02 (0.008)**
Left atrial dimension (n=99,108)	**-0.21 (0.043)**	**-0.12 (0.042)**

No statistical analysis provided for Change From Baseline in Echocardiography (ECHO) Parameters: Left Ventricular End (LVE) Diastolic Diameter, LVE Systolic Diameter, Septal End Diastolic Thickness, Posterior LV Wall End Diastolic Thickness, Relative Wall Thickness, Left Atrial Dimension

5. Secondary: Change From Baseline in Echocardiography Parameters: LVE Diastolic Volume, LVE Systolic Volume, Left Ventricular Stroke Volume, Left Atrial Volume [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Echocardiography Parameters: LVE Diastolic Volume, LVE Systolic Volume, Left Ventricular Stroke Volume, Left Atrial Volume
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A negative change from baseline indicates improvement.
Time Frame	Baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values for each parameter, were included in the analysis for that parameter. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**127**	**125**
Change From Baseline in Echocardiography Parameters: LVE Diastolic Volume, LVE Systolic Volume, Left Ventricular Stroke Volume, Left Atrial Volume [units: ml] Least Squares Mean (Standard Error)		
LVE diastolic volume (n=94,111)	**-12.66 (2.094)**	**-14.31 (2.027)**
LVE systolic volume (n=95,111)	**-8.49 (1.251)**	**-9.64 (1.215)**
LV stroke volume (n=94,111)	**-4.34 (1.448)**	**-4.63 (1.400)**
Left atrial volume (n=96,112)	**-8.08 (2.133)**	**-2.38 (2.057)**

No statistical analysis provided for Change From Baseline in Echocardiography Parameters: LVE Diastolic Volume, LVE Systolic Volume, Left Ventricular Stroke Volume, Left Atrial Volume

6. Secondary: Change From Baseline in Echocardiography Parameters: Left Ventricular Ejection Fraction [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Echocardiography Parameters: Left Ventricular Ejection Fraction
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A negative change from baseline indicates improvement.
Time Frame	Baseline, 36 weeks

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values, were included in the analysis. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**94**	**111**
Change From Baseline in Echocardiography Parameters: Left Ventricular Ejection Fraction [units: Percent ejection fraction] Least Squares Mean (Standard Error)	**2.62 (0.778)**	**2.90 (0.755)**

No statistical analysis provided for Change From Baseline in Echocardiography Parameters: Left Ventricular Ejection Fraction

7. Secondary: Change From Baseline in Echocardiography Parameters: Left Ventricular Mass [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Echocardiography Parameters: Left Ventricular Mass
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A negative change from baseline indicates improvement.
Time Frame	Baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values, were included in the analysis. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	**Valsartan**
Number of Participants Analyzed [units: participants]	**97**	**106**
Change From Baseline in Echocardiography Parameters: Left Ventricular Mass [units: grams (g)] Least Squares Mean (Standard Error)	**-11.26 (4.145)**	**-8.00 (4.106)**

No statistical analysis provided for Change From Baseline in Echocardiography Parameters: Left Ventricular Mass

8. Secondary: Change From Baseline in Echocardiography Parameters: Left Ventricular Mass Index [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Echocardiography Parameters: Left Ventricular Mass Index
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A negative change from baseline indicates improvement.
Time Frame	Baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values, were included in the analysis. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**91**	**100**
Change From Baseline in Echocardiography Parameters: Left Ventricular Mass Index [units: g/m^2] Least Squares Mean (Standard Error)	**-3.95 (2.249)**	**-1.94 (2.283)**

No statistical analysis provided for Change From Baseline in Echocardiography Parameters: Left Ventricular Mass Index

9. Secondary: Change From Baseline in Echocardiography Parameters: Left Atrial Volume Index [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Echocardiography Parameters: Left Atrial Volume Index
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A negative change from baseline indicates improvement.
Time Frame	Baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values, were included in the analysis. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period),

	participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**90**	**106**
Change From Baseline in Echocardiography Parameters: Left Atrial Volume Index [units: ml/m^2] Least Squares Mean (Standard Error)	**-4.02 (1.260)**	**-0.88 (1.237)**

No statistical analysis provided for Change From Baseline in Echocardiography Parameters: Left Atrial Volume Index

10. Secondary: Change From Baseline in Echocardiography Parameters: Ewave Velocity, A Wave Velocity, e' at Septal Mitral Annulus, e' at Lateral Mitral Annulus [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Echocardiography Parameters: Ewave Velocity, A Wave Velocity, e' at Septal Mitral Annulus, e' at Lateral Mitral Annulus
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A negative change from baseline indicates improvement.
Time Frame	Baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values for each parameter, were included in the analysis for that parameter. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	**Valsartan**
Number of Participants Analyzed [units: participants]	**127**	**125**
Change From Baseline in Echocardiography Parameters: Ewave Velocity, A Wave Velocity, e' at Septal Mitral Annulus, e' at Lateral Mitral Annulus [units: cm/s] Least Squares Mean (Standard Error)		
E wave velocity (n=100,112)	**-0.60 (2.947)**	**4.12 (2.897)**
A wave velocity (n=60,68)	**-0.39 (4.199)**	**0.59 (4.265)**
e' at septal mitral annulus (n=79,98)	**1.00 (0.266)**	**0.98 (0.260)**

e' at lateral mitral annulus (n=84,96)	**0.71 (0.307)**	**0.95 (0.296)**

No statistical analysis provided for Change From Baseline in Echocardiography Parameters: Ewave Velocity, A Wave Velocity, e' at Septal Mitral Annulus, e' at Lateral Mitral Annulus

11. Secondary: Change From Baseline in Echocardiography Parameters: Ratio of E to A Velocity, E/e' Ratio [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Echocardiography Parameters: Ratio of E to A Velocity, E/e' Ratio
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A ratio < 1 indicates improvement.
Time Frame	Baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values for each parameter, were included in the analysis for that parameter. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.

Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**127**	**125**
Change From Baseline in Echocardiography Parameters: Ratio of E to A Velocity, E/e' Ratio [units: ratio] Least Squares Mean (Standard Error)		
E to A velocity (n=60,68)	**0.01 (0.080)**	**0.07 (0.081)**
E/e' (n=83,95)	**-1.18 (0.561)**	**-0.75 (0.543)**

No statistical analysis provided for Change From Baseline in Echocardiography Parameters: Ratio of E to A Velocity, E/e' Ratio

12. Secondary: Change in Echocardiography Parameters: Isovolumic Relaxation Time [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change in Echocardiography Parameters: Isovolumic Relaxation Time
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A negative change from baseline indicates improvement.
Time Frame	Baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or

another method. Also provides relevant details such as imputation technique, as appropriate.

Participants from the extension efficacy set, who had both baseline and 36 week values, were included in the analysis. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**35**	**42**
Change in Echocardiography Parameters: Isovolumic Relaxation Time [units: ms] Least Squares Mean (Standard Error)	**0.01 (0.002)**	**0.01 (0.002)**

No statistical analysis provided for Change in Echocardiography Parameters: Isovolumic Relaxation Time

13. Secondary: Change From Baseline in Echocardiography Parameters: Tricuspid Regurgitation Velocity [Time Frame: Baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Echocardiography Parameters: Tricuspid Regurgitation Velocity
Measure Description	A limited two-dimensional and Doppler ECHO examination was done to assess ECHO parameters. A negative change

	from baseline indicates improvement.
Time Frame	Baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values, were included in the analysis. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	**Valsartan**
Number of Participants Analyzed [units: participants]	**35**	**42**
Change From Baseline in Echocardiography Parameters: Tricuspid Regurgitation Velocity [units: m/s] Least Squares Mean (Standard Error)	**-0.05 (0.081)**	**0.00 (0.079)**

No statistical analysis provided for Change From Baseline in Echocardiography Parameters: Tricuspid Regurgitation Velocity

14. Secondary: Change From Baseline in Kansas City Cardiomyopathy Questionnaire (KCCQ) Overall Summary Score and Individual Domain Summary Scores [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Kansas City Cardiomyopathy Questionnaire (KCCQ) Overall Summary Score and Individual Domain Summary Scores
Measure Description	The KCCQ is a self-administered questionnaire. It contains 23 items, covering physical function, clinical symptoms, social function, self-efficacy and knowledge, and quality of life, each with different Likert scale wording, including limitations, frequency, bother, change in condition, understanding, levels of enjoyment and satisfaction. Scores are transformed to a range of 0-100, in which higher scores reflect better health status. A positive change from baseline indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values for each domain, were included in the analysis for that domain. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**127**	**125**
Change From Baseline in Kansas City Cardiomyopathy Questionnaire (KCCQ) Overall Summary Score and Individual Domain Summary Scores [units: score on a scale] Least Squares Mean (Standard Error)		
Physical limitation (n=117,114)	**9.27 (2.528)**	**9.88 (2.516)**
Symptom stability (n=118,116)	**6.43 (3.171)**	**7.94 (3.167)**
Symptom frequency (n=118,116)	**10.38 (2.582)**	**9.16 (2.577)**
Symptom burden (n=118,116)	**9.23 (2.528)**	**9.45 (2.527)**
Total symptom score (n=118,116)	**9.83 (2.386)**	**9.32 (2.384)**
Self efficacy (n=118,116)	**11.24 (2.427)**	**8.77 (2.419)**
Quality of life (n=118,116)	**13.13 (2.706)**	**12.50 (2.702)**
Social limitation (n=113,107)	**9.99 (2.878)**	**11.04 (2.936)**
Overall summary score (n=118,116)	**11.25 (2.185)**	**11.31 (2.183)**

No statistical analysis provided for Change From Baseline in Kansas City Cardiomyopathy Questionnaire (KCCQ) Overall Summary Score and

Individual Domain Summary Scores

15. Secondary: Percentage of Participants With Clinical Composite Assessment of Improved, Unchanged or Worsened [Time Frame: 36 weeks]

Measure Type	Secondary
Measure Title	Percentage of Participants With Clinical Composite Assessment of Improved, Unchanged or Worsened
Measure Description	The clinical composite assessment is defined as follows: Improved = a) participant improved (markedly or moderately) in the global assessment of disease activity with no worsening of NYHA functional class and no major adverse cardiovascular event or b) participant improved in NYHA functional class with no worsening (markedly or moderately) in the global assessment of disease activity and no major adverse cardiovascular event. Worsened = participant worsened (markedly or moderately) in the global assessment of disease activity or in NYHA functional class or experienced a major adverse cardiovascular event. Unchanged = participant does not meet the definition for improved or worsened.
Time Frame	36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Extension efficacy set: the extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.

Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**127**	**125**
Percentage of Participants With Clinical Composite Assessment of Improved, Unchanged or Worsened [units: Percentage of participants]		
Improved	**41.7**	**32.8**
Unchanged	**45.7**	**53.6**
Worsened	**12.6**	**13.6**

No statistical analysis provided for Percentage of Participants With Clinical Composite Assessment of Improved, Unchanged or Worsened

16. Secondary: Percentage of Participants With New York Heart Association (NYHA) Class I, II, II or IV [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Percentage of Participants With New York Heart Association (NYHA) Class I, II, II or IV
Measure Description	The NYHA Functional Classification classifies patients' heart failure according to the severity of their symptoms. The classification is as follows: Class I: no limitation of physical activity, ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath); Class II: slight limitation to physical activity, comfortable at rest, ordinary physical activity results in fatigue, palpitation or dyspnea; Class III: marked limitation of physical activity, comfortable at rest, less than ordinary activity causes fatigue, palpitation or dyspnea; Class IV: unable to carry on any physical activity without discomfort, symptoms of heart failure at rest, if any physical activity is undertaken, discomfort increases.
Time Frame	baseline, 36 weeks

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Extension efficacy set: the extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**127**	**125**
Percentage of Participants With New York Heart Association (NYHA) Class I, II, II or IV [units: Percentage of participants]		
Baseline, Class I	**0.8**	**0.8**
Baseline, Class II	**78.7**	**81.6**
Baseline, Class III	**20.5**	**17.6**
Baseline, Class IV	**0**	**0**
Week 36, Class I	**12.6**	**7.2**

Week 36, Class II	**74.0**	**78.4**
Week 36, Class III	**13.4**	**14.4**
Week 36, Class IV	**0**	**0**

No statistical analysis provided for Percentage of Participants With New York Heart Association (NYHA) Class I, II, II or IV

17. Secondary: Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Estimated Glomerular Filtration Rate (eGFR)
Measure Description	eGFR was calculated from the serum creatinine concentration determined by central laboratory assessment. A positive change from baseline indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values, were included in the analysis for that parameter. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.

Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**126**	**123**
Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) [units: mL/min/1.73m^2] Least Squares Mean (Standard Error)	**-3.68 (1.493)**	**-7.14 (1.517)**

No statistical analysis provided for Change From Baseline in Estimated Glomerular Filtration Rate (eGFR)

18. Secondary: Change From Baseline in Serum Creatinine [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Serum Creatinine
Measure Description	Evaluation of serum creatinine was performed by central laboratory. A negative change from baseline indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Extension efficacy set: the extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**127**	**125**
Change From Baseline in Serum Creatinine [units: µmol/L] Least Squares Mean (Standard Error)	**5.82 (2.136)**	**10.65 (2.183)**

No statistical analysis provided for Change From Baseline in Serum Creatinine

19. Secondary: Change From Baseline in Albumin/Creatinine Ratio [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Albumin/Creatinine Ratio
Measure Description	Evaluation of albumin/creatinine was performed by central laboratory. A ratio < 1 indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the extension efficacy set, who had both baseline and 36 week values, were included in the analysis for that parameter. The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	**Valsartan**
Number of Participants Analyzed [units: participants]	**100**	**101**
Change From Baseline in Albumin/Creatinine Ratio [units: ratio] Geometric Mean (95% Confidence Interval)	**1.19 (0.85 to 1.66)**	**0.74 (0.52 to 1.06)**

No statistical analysis provided for Change From Baseline in Albumin/Creatinine Ratio

20. Secondary: Change From Baseline in Arterial Stiffness Parameters: Brachial Systolic Blood Pressure (SBP), Brachial Diastolic Blood Pressure (DBP), Central Augmentation Pressure, Central Pressure at T1-DP, Central SBP, Central DBP, Central Mean

Pressure [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Arterial Stiffness Parameters: Brachial Systolic Blood Pressure (SBP), Brachial Diastolic Blood Pressure (DBP), Central Augmentation Pressure, Central Pressure at T1-DP, Central SBP, Central DBP, Central Mean Pressure
Measure Description	A vascular arterial stiffness sub-study was conducted in a subset of participants. Noninvasive arterial tonometry was assessed using the Sphygmor device. Participants had arterial stiffness, pulse wave velocity and central pressures measured. A negative change from baseline indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the arterial stiffness set, who had values for both baseline and week 36, were analyzed. The arterial stiffness set included randomized participants who participated in the arterial stiffness sub-study.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	**Valsartan**

Number of Participants Analyzed [units: participants]	**86**	**94**
Change From Baseline in Arterial Stiffness Parameters: Brachial Systolic Blood Pressure (SBP), Brachial Diastolic Blood Pressure (DBP), Central Augmentation Pressure, Central Pressure at T1-DP, Central SBP, Central DBP, Central Mean Pressure [units: mmHg] Least Squares Mean (Standard Error)		
Brachial SBP(n=36,44)	**-1.27 (3.935)**	**1.47 (3.670)**
Brachial DBP (n=36,44)	**1.68 (2.279)**	**0.79 (2.165)**
Central augmentation pressure (n=36,44)	**-0.21 (1.824)**	**-0.24 (1.705)**
Central pressure at T1-DP (n=36,44)	**-1.92 (2.071)**	**0.02 (1.941)**
Central SBP (n=36,44)	**-0.71 (3.856)**	**0.86 (3.594)**
Central DBP (n=36,44)	**1.40 (2.319)**	**0.24 (2.204)**
Central mean pressure (n=36,44)	**0.84 (2.565)**	**-0.13 (2.436)**

No statistical analysis provided for Change From Baseline in Arterial Stiffness Parameters: Brachial Systolic Blood Pressure (SBP), Brachial Diastolic Blood Pressure (DBP), Central Augmentation Pressure, Central Pressure at T1-DP, Central SBP, Central DBP, Central Mean Pressure

21. Secondary: Change From Baseline in Arterial Stiffness Parameters: Heart Rate Correct Cen Aug/Pulse Ht [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Arterial Stiffness Parameters: Heart Rate Correct Cen Aug/Pulse Ht
Measure Description	A vascular arterial stiffness sub-study was conducted in a subset of participants. Noninvasive arterial tonometry was assessed using the Sphygmor device. Participants had arterial stiffness, pulse wave velocity and central pressures measured. A negative change from baseline indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the arterial stiffness set, who had values for both baseline and week 36, were analyzed. The arterial stiffness set included randomized participants who participated in the arterial stiffness sub-study.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**36**	**43**
Change From Baseline in Arterial Stiffness Parameters: Heart Rate Correct Cen Aug/Pulse Ht [units: Percent] Least Squares Mean (Standard Error)	**-0.74 (2.392)**	**-2.16 (2.250)**

No statistical analysis provided for Change From Baseline in Arterial Stiffness Parameters: Heart Rate Correct Cen Aug/Pulse Ht

22. Secondary: Change From Baseline in Arterial Stiffness Parameters: Heart Rate [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Arterial Stiffness Parameters: Heart Rate
Measure Description	A vascular arterial stiffness sub-study was conducted in a subset of participants. Noninvasive arterial tonometry was assessed using the Sphygmor device. Participants had arterial stiffness, pulse wave velocity and central pressures measured. A negative change from baseline indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the arterial stiffness set, who had values for both baseline and week 36, were analyzed. The arterial stiffness set included randomized participants who participated in the arterial stiffness sub-study.

Reporting Groups

	Description

LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**36**	**44**
Change From Baseline in Arterial Stiffness Parameters: Heart Rate [units: bpm] Least Squares Mean (Standard Error)	**-0.64 (2.026)**	**-1.32 (1.905)**

No statistical analysis provided for Change From Baseline in Arterial Stiffness Parameters: Heart Rate

23. Secondary: Change From Baseline in Arterial Stiffness Parameters: Pulse Wave Velocity [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Arterial Stiffness Parameters: Pulse Wave Velocity
Measure Description	A vascular arterial stiffness sub-study was conducted in a subset of participants. Noninvasive arterial tonometry was assessed using the Sphygmor device. Participants had arterial stiffness, pulse wave velocity and central pressures measured. A negative change from baseline indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the arterial stiffness set, who had values for both baseline and week 36, were analyzed. The arterial stiffness set included randomized participants who participated in the arterial stiffness sub-study.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	**Valsartan**
Number of Participants Analyzed [units: participants]	**32**	**42**
Change From Baseline in Arterial Stiffness Parameters: Pulse Wave Velocity [units: cm/s] Least Squares Mean (Standard Error)	**-0.44 (0.731)**	**-0.74 (0.631)**

No statistical analysis provided for Change From Baseline in Arterial Stiffness Parameters: Pulse Wave Velocity

24. Secondary: Change From Baseline in Sitting SBP, Sitting DBP and Sitting Pulse Pressure (PP) [Time Frame: baseline, 36 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Sitting SBP, Sitting DBP and Sitting Pulse Pressure (PP)

Measure Description	Sitting blood pressure and sitting pulse pressure were assessed. A negative change from baseline indicates improvement.
Time Frame	baseline, 36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Extension efficacy set: The extension efficacy set included all randomized participants who had baseline and at least one post-baseline efficacy measurement during the extension period.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Measured Values

	LCZ696	Valsartan
Number of Participants Analyzed [units: participants]	**125**	**127**
Change From Baseline in Sitting SBP, Sitting DBP and Sitting Pulse Pressure (PP) [units: mmHg] Least Squares Mean (Standard Error)		
mean SBP	**-7.47 (1.909)**	**-2.18 (1.936)**
mean DBP	**-5.28 (1.188)**	**-1.39 (1.204)**

Pulse pressure	**-2.24 (1.482)**	**-1.17 (1.497)**

No statistical analysis provided for Change From Baseline in Sitting SBP, Sitting DBP and Sitting Pulse Pressure (PP)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Serious Adverse Events

	LCZ696	Valsartan
Total, serious adverse events		
# participants affected / at risk	**22/149 (14.77%)**	**30/152 (19.74%)**
Blood and lymphatic system disorders		
Anaemia † [1]		
# participants affected / at risk	**2/149 (1.34%)**	**1/152 (0.66%)**

Cardiac disorders		
Acute myocardial infarction † 1		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Angina pectoris † 1		
# participants affected / at risk	**1/149 (0.67%)**	**2/152 (1.32%)**
Angina unstable † 1		
# participants affected / at risk	**3/149 (2.01%)**	**1/152 (0.66%)**
Atrial fibrillation † 1		
# participants affected / at risk	**1/149 (0.67%)**	**1/152 (0.66%)**
Atrioventricular block complete † 1		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Bradyarrhythmia † 1		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Bradycardia † 1		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Cardiac failure † 1		
# participants affected / at risk	**3/149 (2.01%)**	**2/152 (1.32%)**
Cardiac failure acute † 1		
# participants affected / at risk	**1/149 (0.67%)**	**3/152 (1.97%)**
Cardiac failure congestive † 1		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Cardio-respiratory arrest † 1		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Cardiogenic shock † 1		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**

Coronary artery stenosis † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Myocardial infarction † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Palpitations † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Sick sinus syndrome † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Tachyarrhythmia † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Ear and labyrinth disorders		
Vertigo † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Gastrointestinal disorders		
Ascites † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Diarrhoea † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Diarrhoea haemorrhagic † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Duodenal ulcer † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Gastric haemorrhage † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**2/152 (1.32%)**
Gastritis † [1]		

# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
Gastritis erosive † 1		
# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
Ileus † 1		
# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
Melaena † 1		
# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
General disorders		
Asthenia † 1		
# participants affected / at risk	2/149 (1.34%)	0/152 (0.00%)
Chest discomfort † 1		
# participants affected / at risk	1/149 (0.67%)	0/152 (0.00%)
Device malfunction † 1		
# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
Non-cardiac chest pain † 1		
# participants affected / at risk	1/149 (0.67%)	1/152 (0.66%)
Oedema peripheral † 1		
# participants affected / at risk	1/149 (0.67%)	0/152 (0.00%)
Pyrexia † 1		
# participants affected / at risk	0/149 (0.00%)	2/152 (1.32%)
Hepatobiliary disorders		
Cholelithiasis † 1		
# participants affected / at risk	1/149 (0.67%)	0/152 (0.00%)
Infections and infestations		
Appendicitis † 1		

# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
Bacterial sepsis † 1		
# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
Bronchitis † 1		
# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
Endocarditis † 1		
# participants affected / at risk	1/149 (0.67%)	0/152 (0.00%)
Gastroenteritis † 1		
# participants affected / at risk	1/149 (0.67%)	0/152 (0.00%)
Pneumonia † 1		
# participants affected / at risk	1/149 (0.67%)	1/152 (0.66%)
Postoperative wound infection † 1		
# participants affected / at risk	1/149 (0.67%)	0/152 (0.00%)
Sepsis † 1		
# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
Urinary tract infection † 1		
# participants affected / at risk	0/149 (0.00%)	2/152 (1.32%)
Injury, poisoning and procedural complications		
Humerus fracture † 1		
# participants affected / at risk	1/149 (0.67%)	0/152 (0.00%)
Lower limb fracture † 1		
# participants affected / at risk	0/149 (0.00%)	1/152 (0.66%)
Spinal fracture † 1		
# participants affected / at risk	1/149 (0.67%)	0/152 (0.00%)
Metabolism and nutrition disorders		

Diabetes mellitus inadequate control † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Hyperglycaemia † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Hyperkalaemia † [1]		
# participants affected / at risk	**2/149 (1.34%)**	**1/152 (0.66%)**
Musculoskeletal and connective tissue disorders		
Back pain † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Muscular weakness † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Osteoarthritis † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Osteonecrosis † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Adrenal carcinoma † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Pancreatic carcinoma † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Nervous system disorders		
Carotid artery stenosis † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Cerebrovascular insufficiency † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**

Syncope † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Transient ischaemic attack † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Renal and urinary disorders		
Hyperuricosuria † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Renal colic † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Renal failure † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Renal failure acute † [1]		
# participants affected / at risk	**2/149 (1.34%)**	**1/152 (0.66%)**
Urinary retention † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Respiratory, thoracic and mediastinal disorders		
Acute pulmonary oedema † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Bronchiectasis † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Dyspnoea † [1]		
# participants affected / at risk	**2/149 (1.34%)**	**4/152 (2.63%)**
Productive cough † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**3/152 (1.97%)**
Pulmonary oedema † [1]		

# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Respiratory failure † 1		
# participants affected / at risk	**0/149 (0.00%)**	**2/152 (1.32%)**
Skin and subcutaneous tissue disorders		
Angioedema † 1		
# participants affected / at risk	**1/149 (0.67%)**	**0/152 (0.00%)**
Vascular disorders		
Arterial thrombosis limb † 1		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Femoral arterial stenosis † 1		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Hypotension † 1		
# participants affected / at risk	**2/149 (1.34%)**	**1/152 (0.66%)**
Peripheral arterial occlusive disease † 1		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**
Peripheral embolism † 1		
# participants affected / at risk	**0/149 (0.00%)**	**1/152 (0.66%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	2%

Reporting Groups

	Description
LCZ696	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 50 mg LCZ696 for 1- 2 weeks, then uptitrated to 100 mg bid for 1 -2 weeks, and thereafter, uptitrated to 200 mg bid.
Valsartan	During a single blind, run-in period, participants received placebo. Then at randomization (double blind treatment period), participants started with 40 mg Valsartan twice daily (bid) for 1 - 2 weeks, then were uptitrated to 80 mg bid for 1 -2 weeks, and thereafter, uptitrated to 160 mg bid.

Other Adverse Events

	LCZ696	Valsartan
Total, other (not including serious) adverse events		
# participants affected / at risk	**79/149 (53.02%)**	**92/152 (60.53%)**
Blood and lymphatic system disorders		
Anaemia † [1]		
# participants affected / at risk	**2/149 (1.34%)**	**5/152 (3.29%)**
Cardiac disorders		
Angina pectoris † [1]		
# participants affected / at risk	**4/149 (2.68%)**	**2/152 (1.32%)**
Atrial fibrillation † [1]		
# participants affected / at risk	**2/149 (1.34%)**	**8/152 (5.26%)**
Bradycardia † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**4/152 (2.63%)**

Cardiac failure † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**4/152 (2.63%)**
Cardiac failure chronic † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**4/152 (2.63%)**
Palpitations † [1]		
# participants affected / at risk	**5/149 (3.36%)**	**5/152 (3.29%)**
Ear and labyrinth disorders		
Vertigo † [1]		
# participants affected / at risk	**5/149 (3.36%)**	**1/152 (0.66%)**
Eye disorders		
Cataract † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**1/152 (0.66%)**
Gastrointestinal disorders		
Abdominal pain † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**3/152 (1.97%)**
Constipation † [1]		
# participants affected / at risk	**2/149 (1.34%)**	**5/152 (3.29%)**
Diarrhoea † [1]		
# participants affected / at risk	**9/149 (6.04%)**	**4/152 (2.63%)**
Dyspepsia † [1]		
# participants affected / at risk	**4/149 (2.68%)**	**2/152 (1.32%)**
Nausea † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**4/152 (2.63%)**
General disorders		
Asthenia † [1]		

# participants affected / at risk	**7/149 (4.70%)**	**10/152 (6.58%)**
Fatigue † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**6/152 (3.95%)**
Non-cardiac chest pain † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**0/152 (0.00%)**
Oedema peripheral † [1]		
# participants affected / at risk	**4/149 (2.68%)**	**9/152 (5.92%)**
Pyrexia † [1]		
# participants affected / at risk	**4/149 (2.68%)**	**0/152 (0.00%)**
Infections and infestations		
Bronchitis † [1]		
# participants affected / at risk	**6/149 (4.03%)**	**2/152 (1.32%)**
Gastroenteritis † [1]		
# participants affected / at risk	**4/149 (2.68%)**	**1/152 (0.66%)**
Influenza † [1]		
# participants affected / at risk	**4/149 (2.68%)**	**5/152 (3.29%)**
Nasopharyngitis † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**5/152 (3.29%)**
Respiratory tract infection † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**4/152 (2.63%)**
Upper respiratory tract infection † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**1/152 (0.66%)**
Urinary tract infection † [1]		
# participants affected / at risk	**6/149 (4.03%)**	**9/152 (5.92%)**
Metabolism and nutrition disorders		

Dyslipidaemia † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**0/152 (0.00%)**
Gout † [1]		
# participants affected / at risk	**0/149 (0.00%)**	**4/152 (2.63%)**
Hyperkalaemia † [1]		
# participants affected / at risk	**10/149 (6.71%)**	**8/152 (5.26%)**
Hypokalaemia † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**1/152 (0.66%)**
Musculoskeletal and connective tissue disorders		
Arthralgia † [1]		
# participants affected / at risk	**5/149 (3.36%)**	**2/152 (1.32%)**
Back pain † [1]		
# participants affected / at risk	**5/149 (3.36%)**	**4/152 (2.63%)**
Pain in extremity † [1]		
# participants affected / at risk	**5/149 (3.36%)**	**2/152 (1.32%)**
Nervous system disorders		
Dizziness † [1]		
# participants affected / at risk	**11/149 (7.38%)**	**7/152 (4.61%)**
Headache † [1]		
# participants affected / at risk	**3/149 (2.01%)**	**4/152 (2.63%)**
Psychiatric disorders		
Insomnia † [1]		
# participants affected / at risk	**1/149 (0.67%)**	**4/152 (2.63%)**
Renal and urinary disorders		
Renal impairment † [1]		

# participants affected / at risk	**1/149 (0.67%)**	**5/152 (3.29%)**
Respiratory, thoracic and mediastinal disorders		
Cough † 1		
# participants affected / at risk	**9/149 (6.04%)**	**8/152 (5.26%)**
Dyspnoea † 1		
# participants affected / at risk	**4/149 (2.68%)**	**11/152 (7.24%)**
Skin and subcutaneous tissue disorders		
Pruritus † 1		
# participants affected / at risk	**2/149 (1.34%)**	**5/152 (3.29%)**
Vascular disorders		
Hypertension † 1		
# participants affected / at risk	**3/149 (2.01%)**	**6/152 (3.95%)**
Hypotension † 1		
# participants affected / at risk	**19/149 (12.75%)**	**14/152 (9.21%)**
Orthostatic hypotension † 1		
# participants affected / at risk	**2/149 (1.34%)**	**5/152 (3.29%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. ☑ **Restriction Description:** The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial or disclosure of trial results in their entirety.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862-778-8300

Publications:

Solomon SD, Zile M, Pieske B, Voors A, Shah A, Kraigher-Krainer E, Shi V, Bransford T, Takeuchi M, Gong J, Lefkowitz M, Packer M, McMurray JJ; Prospective comparison of ARNI with ARB on Management Of heart failUre with preserved ejectioN fracTion (PARAMOUNT) Investigators.

The angiotensin receptor neprilysin inhibitor LCZ696 in heart failure with preserved ejection fraction: a phase 2 double-blind randomised controlled trial. Lancet. 2012 Oct 20;380(9851):1387-95. doi: 10.1016/S0140-6736(12)61227-6. Epub 2012 Aug 26.

Publications automatically indexed to this study:

Jhund PS, Claggett BL, Voors AA, Zile MR, Packer M, Pieske BM, Kraigher-Krainer E, Shah AM, Prescott MF, Shi V, Lefkowitz M, McMurray JJ, Solomon SD; PARAMOUNT Investigators. Elevation in high-sensitivity troponin T in heart failure and preserved ejection fraction and influence of treatment with the angiotensin receptor neprilysin inhibitor LCZ696. Circ Heart Fail. 2014 Nov;7(6):953-9. doi: 10.1161/CIRCHEARTFAILURE.114.001427. Epub 2014 Oct 2.

Santos AB, Kraigher-Krainer E, Gupta DK, Claggett B, Zile MR, Pieske B, Voors AA, Lefkowitz M, Bransford T, Shi V, Packer M, McMurray JJ, Shah AM, Solomon SD; PARAMOUNT Investigators. Impaired left atrial function in heart failure with preserved ejection fraction. Eur J Heart Fail. 2014 Oct;16(10):1096-103. doi: 10.1002/ejhf.147. Epub 2014 Aug 19.

Kraigher-Krainer E, Shah AM, Gupta DK, Santos A, Claggett B, Pieske B, Zile MR, Voors AA, Lefkowitz MP, Packer M, McMurray JJ, Solomon SD; PARAMOUNT Investigators. Impaired systolic function by strain imaging in heart failure with preserved ejection fraction. J Am Coll Cardiol. 2014 Feb 11;63(5):447-56. doi: 10.1016/j.jacc.2013.09.052. Epub 2013 Oct 30. Erratum in: J Am Coll Cardiol. 2014 Jul 22;64(3):335.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00887588 History of Changes
Other Study ID Numbers:	**CLCZ696B2214** 2009-010208-27
Study First Received:	April 22, 2009
Results First Received:	July 16, 2015
Last Updated:	August 12, 2015
Health Authority:	United States: Food and Drug Administration Argentina: Ministry of Health Brazil: Ministry of Health Canada: Health Canada India: Ministry of Health Italy: Ministry of Health Netherlands: Medicines Evaluation Board (MEB) Poland: Ministry of Health Romania: Ministry of Public Health Russia: Pharmacological Committee, Ministry of Health Singapore: Health Sciences Authority Spain: Ministry of Health

Venezuela: Ministry of Health and Social Development
Germany: Federal Institute for Drugs and Medical Devices