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Trial record **1 of 1** for: CLCZ696B2203

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A Study of LCZ696 in Subjects With Mild and Moderate Hepatic Impairment Compared With Normal Healthy Volunteers

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

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

ClinicalTrials.gov Identifier:
NCT01621633

First received: June 14, 2012
Last updated: July 11, 2015
Last verified: July 2015
History of Changes

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Results First Received: July 11, 2015

Study Type:	Interventional
Study Design:	Allocation: Non-Randomized; Endpoint Classification: Pharmacokinetics Study; Intervention Model: Parallel Assignment; Masking: Open Label
Condition:	Hepatic Impairment
Intervention:	Drug: LCZ696

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
Participants received the study treatment according to the population subset that was defined based on the severity of hepatic impairment and healthy volunteers: Group 1, subjects with mild hepatic impairment; Group 2, subjects with moderate hepatic impairment; Groups 3 and 4, healthy volunteers matching to Groups 1 and 2, respectively.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Participants With Mild Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Participants With Moderate Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Healthy Volunteers (Mild HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 1
Healthy Volunteers (Moderate HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 2

Participant Flow: Overall Study

	Participants With Mild Hepatic Impairment (HI)	Participants With Moderate Hepatic Impairment (HI)	Healthy Volunteers (Mild HI Matched)	Healthy Volunteers (Moderate HI Matched)
STARTED	8	8	8	8
COMPLETED	8	8	8	8

NOT COMPLETED	**0**	**0**	**0**	**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
Participants With Mild Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Participants With Moderate Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Healthy Volunteers (Mild HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 1
Healthy Volunteers (Moderate HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 2
Total	Total of all reporting groups

Baseline Measures

	Participants With Mild Hepatic Impairment (HI)	Participants With Moderate Hepatic Impairment (HI)	Healthy Volunteers (Mild HI Matched)	Healthy Volunteers (Moderate HI Matched)	Total
Number of					

Participants [units: participants]	**8**	**8**	**8**	**8**	**32**
Age [units: Years] Mean (Standard Deviation)	**59.1 (7.92)**	**57.9 (11.67)**	**58.9 (8.68)**	**60.3 (11.21)**	**59.0 (9.54)**
Gender [units: Participants]					
Female	**3**	**1**	**3**	**1**	**8**
Male	**5**	**7**	**5**	**7**	**24**

Outcome Measures

Hide All Outcome Measures

1. Primary: Area Under the Plasma Concentration-time Profile From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of LCZ696 Analytes (AHU377, LBQ657, and Valsartan) [Time Frame: From pre-dose on Day 1 until 96h post-dose (Day 5)]

Measure Type	Primary
Measure Title	Area Under the Plasma Concentration-time Profile From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of LCZ696 Analytes (AHU377, LBQ657, and Valsartan)
Measure Description	Blood samples were taken on Day 1 (treatment day) within 60 minutes prior to dosing, then, 0.5,1,1.5,2,3,4,6,8,12 hours after the dosing and on Days 2, 3, 4 and 5 post dosing
Time Frame	From pre-dose on Day 1 until 96h post-dose (Day 5)
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.

PK analysis set: The PK analysis set included all subjects with at least one available, valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug, and experienced no protocol deviations with relevant impact on PK data.

Reporting Groups

	Description
Participants With Mild Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Participants With Moderate Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Healthy Volunteers (Mild HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 1
Healthy Volunteers (Moderate HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 2

Measured Values

	Participants With Mild Hepatic Impairment (HI)	Participants With Moderate Hepatic Impairment (HI)	Healthy Volunteers (Mild HI Matched)	Healthy Volunteers (Moderate HI Matched)
Number of Participants Analyzed [units: participants]	**8**	**8**	**8**	**8**
Area Under the Plasma Concentration-time Profile From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of LCZ696 Analytes (AHU377, LBQ657, and Valsartan) [units: ng*hr/mL] Mean (Standard Deviation)				
AHU377	**2540 (1010)**	**6200 (2970)**	**1580 (390)**	**1740 (520)**
LBQ657	**118000 (37000)**	**173000 (99900)**	**77900 (14700)**	**83100 (14700)**
			21600	**25300 (11800)**

Valsartan	**28500 (16900)**	**63800 (48700)**	**(5980)**	

No statistical analysis provided for Area Under the Plasma Concentration-time Profile From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of LCZ696 Analytes (AHU377, LBQ657, and Valsartan)

2. Primary: Area Under the Plasma Concentration-time Profile From Time Zero Extrapolated to Infinite Time [AUCinf)] of LCZ696 Analytes (AHU377, LBQ657, and Valsartan) [Time Frame: From pre-dose on Day 1 until 96h post-dose (Day 5)]

Measure Type	Primary
Measure Title	Area Under the Plasma Concentration-time Profile From Time Zero Extrapolated to Infinite Time [AUCinf)] of LCZ696 Analytes (AHU377, LBQ657, and Valsartan)
Measure Description	Blood samples were taken on Day 1 (treatment day) within 60 minutes prior to dosing, then, 0.5,1,1.5,2,3,4,6,8,12 hours after the dosing and on Days 2, 3, 4 and 5 post dosing
Time Frame	From pre-dose on Day 1 until 96h post-dose (Day 5)
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.
PK analysis set

Reporting Groups

	Description
Participants With Mild Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Participants With Moderate Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Healthy Volunteers (Mild HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment

	in group 1
Healthy Volunteers (Moderate HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 2

Measured Values

	Participants With Mild Hepatic Impairment (HI)	Participants With Moderate Hepatic Impairment (HI)	Healthy Volunteers (Mild HI Matched)	Healthy Volunteers (Moderate HI Matched)
Number of Participants Analyzed [units: participants]	**8**	**8**	**8**	**8**
Area Under the Plasma Concentration-time Profile From Time Zero Extrapolated to Infinite Time [AUCinf)] of LCZ696 Analytes (AHU377, LBQ657, and Valsartan) [units: ng*hr/mL] Mean (Standard Deviation)				
AHU377	**2540 (1010)**	**6200 (2980)**	**1590 (390)**	**1740 (519)**
LBQ657	**121000 (41000)**	**187000 (124000)**	**78500 (14700)**	**84100 (14800)**
Valsartan	**28800 (16900)**	**65600 (50100)**	**21900 (5950)**	**26500 (12400)**

No statistical analysis provided for Area Under the Plasma Concentration-time Profile From Time Zero Extrapolated to Infinite Time [AUCinf)] of LCZ696 Analytes (AHU377, LBQ657, and Valsartan)

3. Primary: Maximum Plasma Concentration (Cmax) for LCZ696 Analytes (AHU377, LBQ657, and Valsartan) [Time Frame: From pre-dose on Day 1 until 96h post-dose (Day 5)]

Measure Type	Primary

Measure Title	Maximum Plasma Concentration (Cmax) for LCZ696 Analytes (AHU377, LBQ657, and Valsartan)
Measure Description	Blood samples were taken on Day 1 (treatment day) within 60 minutes prior to dosing, then, 0.5,1,1.5,2,3,4,6,8,12 hours after the dosing and on Days 2, 3, 4 and 5 post dosing
Time Frame	From pre-dose on Day 1 until 96h post-dose (Day 5)
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.
PK analysis set

Reporting Groups

	Description
Participants With Mild Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Participants With Moderate Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Healthy Volunteers (Mild HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 1
Healthy Volunteers (Moderate HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 2

Measured Values

	Participants With Mild Hepatic Impairment (HI)	**Participants With Moderate Hepatic Impairment (HI)**	**Healthy Volunteers (Mild HI Matched)**	**Healthy Volunteers (Moderate HI Matched)**
Number of Participants Analyzed [units: participants]	**8**	**8**	**8**	**8**

Maximum Plasma Concentration (Cmax) for LCZ696 Analytes (AHU377, LBQ657, and Valsartan) [units: ng/mL] Mean (Standard Deviation)				
AHU377	**2530 (1400)**	**4430 (1760)**	**1510 (585)**	**1410 (445)**
LBQ657	**7730 (1470)**	**6690 (917)**	**7450 (1320)**	**6770 (1710)**
Valsartan	**4000 (2310)**	**4180 (2340)**	**3880 (1490)**	**3730 (1540)**

No statistical analysis provided for Maximum Plasma Concentration (Cmax) for LCZ696 Analytes (AHU377, LBQ657, and Valsartan)

4. Secondary: Number of Participants With Adverse Events, Serious Adverse Events and Death [Time Frame: From the screening visit until Day 5]

Measure Type	Secondary
Measure Title	Number of Participants With Adverse Events, Serious Adverse Events and Death
Measure Description	Adverse events, serious adverse events and death were monitored from screening to end of study
Time Frame	From the screening visit until Day 5
Safety Issue	Yes

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.
Safety set: The safety set includes all participants who received study treatment.

Reporting Groups

	Description

Participants With Mild Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Participants With Moderate Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose
Healthy Volunteers (Mild HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 1
Healthy Volunteers (Moderate HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 2

Measured Values

	Participants With Mild Hepatic Impairment (HI)	Participants With Moderate Hepatic Impairment (HI)	Healthy Volunteers (Mild HI Matched)	Healthy Volunteers (Moderate HI Matched)
Number of Participants Analyzed [units: participants]	**8**	**8**	**8**	**8**
Number of Participants With Adverse Events, Serious Adverse Events and Death [units: Participants]				
Adverse events (serious and non-serious)	**0**	**2**	**0**	**0**
Serious adverse events	**0**	**0**	**0**	**0**
Deaths	**0**	**0**	**0**	**0**

No statistical analysis provided for Number of Participants With Adverse Events, Serious Adverse Events and Death

Serious Adverse Events

Hide Serious Adverse Events

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

Reporting Groups

	Description
Moderate Hepatic Impaired Patients	Moderate hepatic impaired patients
Healthy Volunteers (Mild HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 1
Healthy Volunteers (Moderate HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 2
Participants With Mild Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose

Serious Adverse Events

	Moderate Hepatic Impaired Patients	Healthy Volunteers (Mild HI Matched)	Healthy Volunteers (Moderate HI Matched)	Participants With Mild Hepatic Impairment (HI)
Total, serious adverse events				
# participants affected / at risk	**0/8 (0.00%)**	**0/8 (0.00%)**	**0/8 (0.00%)**	**0/8 (0.00%)**

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	5%

Reporting Groups

	Description
Moderate Hepatic Impaired Patients	Moderate hepatic impaired patients
Healthy Volunteers (Mild HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 1
Healthy Volunteers (Moderate HI Matched)	LCZ696 200 mg, given as a single oral dose. Each healthy volunteer matched in race, age (±5 years), gender, weight (±15%) to an individual subject with hepatic impairment in group 2
Participants With Mild Hepatic Impairment (HI)	LCZ696 200 mg, given as a single oral dose

Other Adverse Events

	Moderate Hepatic Impaired Patients	Healthy Volunteers (Mild HI Matched)	Healthy Volunteers (Moderate HI Matched)	Participants With Mild Hepatic Impairment (HI)
Total, other (not including serious) adverse events				
# participants affected / at risk	**2/8 (25.00%)**	**0/8 (0.00%)**	**0/8 (0.00%)**	**0/8 (0.00%)**
Gastrointestinal disorders				
DIARRHOEA † [1]				
# participants affected / at risk	**1/8 (12.50%)**	**0/8 (0.00%)**	**0/8 (0.00%)**	**0/8 (0.00%)**
Investigations				
BLOOD POTASSIUM DECREASED † [1]				
# participants affected /				

at risk	**1/8 (12.50%)**	**0/8 (0.00%)**	**0/8 (0.00%)**	**0/8 (0.00%)**
Renal and urinary disorders				
RENAL IMPAIRMENT † 1				
# participants affected / at risk	**1/8 (12.50%)**	**0/8 (0.00%)**	**0/8 (0.00%)**	**0/8 (0.00%)**

† 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

No publications provided

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT01621633 History of Changes
Other Study ID Numbers:	**CLCZ696B2203**
	2012-000983-27 (EudraCT Number)
Study First Received:	June 14, 2012
Results First Received:	July 11, 2015
Last Updated:	July 11, 2015
Health Authority:	Germany: Federal Institute for Drugs and Medical Devices