Clinical trial results:
A multicenter, open-label study to collect the safety information of sacubitril/valsartan in Japanese pediatric patients with heart failure due to systemic left ventricle systolic dysfunction who have completed CLCZ696B2319E1 study

Summary

EudraCT number	2023-001004-33
Trial protocol	Outside EU/EEA
Global end of trial date	14 August 2024

Results information

Result version number	v1 (current)
This version publication date	12 February 2025
First version publication date	12 February 2025

Trial information

Trial identification

Sponsor protocol code	CLCZ696B2319E2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT06149104
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Novartis Pharma AG, Clinical Disclosure Office, 41 613241111, novartis.email@novartis.com
Scientific contact	Novartis Pharma AG, Clinical Disclosure Office, 41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To collect additional safety information of sacubitril/valsartan in Japanese patients after long-term treatment of sacubitril/valsartan in CLCZ696B2319E1 study.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2023
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 8
Worldwide total number of subjects	8
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	7
Adolescents (12-17 years)	1
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 6 investigative sites in Japan.

Pre-assignment

Screening details:

All consenting participants were assessed for eligibility into this study at the first visit (Visit Day 1) and the study medication was initiated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Sacubitril/Valsartan

Arm description:

The starting dose of study drug was determined by the investigator in consideration of the participant´s condition. The dose level at the end of study visit of CLCZ696B2319E1 study could remain the same, or the dose level could be changed at the discretion of the investigator. All participants had a target dose of 3.1 mg/kg bid. If a participant was unable to tolerate up-titration to a higher sacubitril/valsartan dose level or at the discretion of the Investigator, participants could be maintained on lower dose levels of sacubitril/valsartan.

Arm type	Experimental
Investigational medicinal product name	Sacubitril/Valsartan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The starting dose of study drug was determined by the investigator in consideration of the participant´s condition. The dose level at the end of study visit of CLCZ696B2319E1 study could remain the same, or the dose level could be changed at the discretion of the investigator.

Investigational medicinal product name	Sacubitril/Valsartan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The starting dose of study drug was determined by the investigator in consideration of the participant´s condition. The dose level at the end of study visit of CLCZ696B2319E1 study could remain the same, or the dose level could be changed at the discretion of the investigator.

Investigational medicinal product name	Sacubitril/Valsartan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

The starting dose of study drug was determined by the investigator in consideration of the participant´s condition. The dose level at the end of study visit of CLCZ696B2319E1 study could remain the same, or the dose level could be changed at the discretion of the investigator.

Number of subjects in period 1	Sacubitril/Valsartan
Started	8
Completed	8

Baseline characteristics

Reporting groups	
Reporting group title	Sacubitril/Valsartan

Reporting group description:

The starting dose of study drug was determined by the investigator in consideration of the participant´s condition. The dose level at the end of study visit of CLCZ696B2319E1 study could remain the same, or the dose level could be changed at the discretion of the investigator. All participants had a target dose of 3.1 mg/kg bid. If a participant was unable to tolerate up-titration to a higher sacubitril/valsartan dose level or at the discretion of the Investigator, participants could be maintained on lower dose levels of sacubitril/valsartan.

Reporting group values	Sacubitril/Valsartan	Total	
Number of subjects	8	8	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	7	7	
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	6.75		
standard deviation	± 4.234	-	
Sex: Female, Male Units: participants			
Female	6	6	
Male	2	2	
Race/Ethnicity, Customized Units: Subjects			
Asian	8	8	

End points

End points reporting groups

Reporting group title	Sacubitril/Valsartan

Reporting group description:

The starting dose of study drug was determined by the investigator in consideration of the participant´s condition. The dose level at the end of study visit of CLCZ696B2319E1 study could remain the same, or the dose level could be changed at the discretion of the investigator. All participants had a target dose of 3.1 mg/kg bid. If a participant was unable to tolerate up-titration to a higher sacubitril/valsartan dose level or at the discretion of the Investigator, participants could be maintained on lower dose levels of sacubitril/valsartan.

Primary: Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)[1]

End point description:

Number of participants with treatment emergent adverse events (any AE regardless of seriousness), and SAEs.

End point type	Primary

End point timeframe:

Adverse events were reported from first dose of study treatment until end of study treatment, up to a maximum duration of approximately 8 months.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only analyzed descriptively.

End point values	Sacubitril/Valsartan			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: participants				
Adverse Events	6			
Serious Adverse Events	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment, up to a maximum duration of approximately 8 months.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Sacubitril/Valsartan

Reporting group description:

Sacubitril/Valsartan

Reporting group title	All Patients

Reporting group description:

All Patients

Serious adverse events	Sacubitril/Valsartan	All Patients	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Sacubitril/Valsartan	All Patients	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	6 / 8 (75.00%)	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	3	3	
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Muscle tightness			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Gastroenteritis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Influenza			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	2 / 8 (25.00%)	2 / 8 (25.00%)	
occurrences (all)	5	5	
Otitis media			

subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Streptococcal infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported