EU Clinical Trials Register

Clinical trial results:
A multicenter, open-label Phase 3 study: ambulatory blood pressure monitoring in adult patients with chronic spontaneous urticaria inadequately controlled by H1-antihistamines treated with remibrutinib up to 12 weeks

Summary

EudraCT number	2022-002838-13
Trial protocol	ES SK DE
Global end of trial date	25 April 2024

Results information

Result version number	v1 (current)
This version publication date	26 April 2025
First version publication date	26 April 2025

Trial information

Trial identification

Sponsor protocol code	CLOU064A2305

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05795153
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to assess the effect of remibrutinib 25 mg b.i.d. open-label on SBP measured as a change in 24-hour weighted average SBP from baseline to Week 4 assessed by ABPM; and to assess overall safety and efficacy over 12 weeks in adult participants with CSU inadequately controlled with second generation H1-AH treatment.

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	05 April 2023
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 8
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	France: 32
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Korea, Republic of: 15
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Slovakia: 11
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Türkiye: 10
Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	144
EEA total number of subjects	73

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	131
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted globally across 10 countries: Argentina (4 centers), Canada (2 centers), France (8 centers), Germany (6 centers), Republic of Korea/South Korea (3 centers), Singapore (1 center), Slovakia (3 centers), Spain (4 centers), Turkey (3 centers), and USA (11 centers).

Pre-assignment

Screening details:

Participants underwent a screening period of up to 4 weeks.

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	LOU064 (remibrutinib)

Arm description:

All participants were assigned to remibrutinib 25 mg b.i.d. for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Remibrutinib
Investigational medicinal product code	LOU064
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One film-coated tablet (25 mg) was to be taken in the morning and evening, respectively, with a 12-hour interval at approximately the same time everyday

Number of subjects in period 1	LOU064 (remibrutinib)
Started	144
Completed	137
Not completed	7
Adverse event, non-fatal	2
Subject decision	2
Unsatisfactory therapeutic effect	2
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	LOU064 (remibrutinib)
Reporting group description:	
All participants were assigned to remibrutinib 25 mg b.i.d. for 12 weeks.	

Reporting group values	LOU064 (remibrutinib)	Total	
Number of subjects	144	144	
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	131	131	
From 65-84 years	13	13	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	42.2		
standard deviation	± 14.52	-	
Sex: Female, Male			
Units: Participants			
Female	105	105	
Male	39	39	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	19	19	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	3	3	
White	89	89	
More than one race	0	0	
Unknown or Not Reported	32	32	
Baseline Systolic Blood Pressure (SBP)			
Units: millimeter of mercury (mmHg)			
arithmetic mean	117.1		
standard deviation	± 13.11	-	
Baseline Diastolic Blood Pressure (DBP)			
Units: millimeter of mercury (mmHg)			
arithmetic mean	75.0		
standard deviation	± 8.98	-	

End points

End points reporting groups

Reporting group title	LOU064 (remibrutinib)
Reporting group description:	
All participants were assigned to remibrutinib 25 mg b.i.d. for 12 weeks.	

Primary: Estimated Mean Change from Baseline at Week 4 in 24-hour Systolic Blood Pressure (SBP) measured by Ambulatory Blood Pressure Monitoring (ABPM)

End point title	Estimated Mean Change from Baseline at Week 4 in 24-hour Systolic Blood Pressure (SBP) measured by Ambulatory Blood Pressure Monitoring (ABPM)[1]

End point description:

A linear regression with SBP as a covariate was employed. The change in SBP from baseline to Week 4 was predicted at the median baseline level. The change from baseline in the 24-hour weighted average SBP was calculated using the time weighted average of the area under the curve (AUC) of SBP obtained over a 24-hour period as measured by ABPM. That is, the time weighted average of AUC of 24-hour SBP obtained at baseline was subtracted from corresponding time weighted average of AUC of SBP at Week 4.

In the analysis, if participants took prohibited antihypertensive treatment before Week 4, their subsequent measurements were excluded. In such cases, the excluded measurements were imputed by increasing the 24-hour SBP by 3 mmHg from the baseline value at Week 4. Moreover, participants who discontinued of study treatment due to any reason prior to the Week 4 were excluded from the analysis. The Mixed Models for Repeated Measures (MMRM) approach was used.

End point type	Primary
End point timeframe:	
Baseline, Week 4	

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: No statistical analyses were planned for the primary endpoint

End point values	LOU064 (remibrutinib)			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: millimeter of mercury (mmHg)				
arithmetic mean (confidence interval 95%)	-1.3 (-2.3 to -0.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Mean Change from Baseline to Week 4 in 24-hour weighted average Systolic Blood Pressure (SBP) measured by ABPM

End point title	Observed Mean Change from Baseline to Week 4 in 24-hour weighted average Systolic Blood Pressure (SBP) measured by ABPM

End point description:

The change from baseline in the 24-hour weighted average systolic blood pressure (SBP) was calculated

using the time weighted average of the area under the curve (AUC) of SBP obtained over a 24-hour period as measured by ABPM. This analysis was conducted using the observed data.

Data was computed taking weighted averages over time and discarding time intervals of more than 1 hour without measurements.

End point type	Secondary
End point timeframe:	
Baseline, Week 4	

End point values	LOU064 (remibrutinib)			
Subject group type	Reporting group			
Number of subjects analysed	142			
Units: millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)	-1.65 (± 6.905)			

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated Mean Change from Baseline at Week 4 in 24-hour Diastolic Blood Pressure (DBP) measured by ABPM

End point title	Estimated Mean Change from Baseline at Week 4 in 24-hour Diastolic Blood Pressure (DBP) measured by ABPM

End point description:

A linear regression with DBP as a covariate was employed. The change in DBP from baseline to Week 4 was predicted at the median baseline level. The change from baseline in the 24-hour weighted average DBP was calculated using the time weighted average of the area under the curve (AUC) of DBP obtained over a 24-hour period as measured by ABPM. That is, the time weighted average of AUC of 24-hour DBP obtained at baseline was subtracted from corresponding time weighted average of AUC of DBP at Week 4.

In the analysis, if participants took prohibited antihypertensive treatment before Week 4, their subsequent measurements were excluded. In such cases, the excluded measurements were imputed by increasing the 24-hour DBP by 3 mmHg from the baseline value at Week 4. Moreover, participants who discontinued of study treatment due to any reason prior to the Week 4 were excluded from the analysis. The Mixed Models for Repeated Measures (MMRM) approach was used.

End point type	Secondary
End point timeframe:	
Baseline, Week 4	

End point values	LOU064 (remibrutinib)			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: millimeter of mercury (mmHg)				
arithmetic mean (confidence interval 95%)	-0.1 (-0.8 to 0.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated Mean Change from Baseline at Week 4 in daytime and nighttime average SBP measured by ABPM

End point title	Estimated Mean Change from Baseline at Week 4 in daytime and nighttime average SBP measured by ABPM

End point description:

The change in daytime (respectively nighttime) weighted average SBP was analyzed using linear regression model with baseline weighted average daytime SBP (respectively nighttime) as a covariate. The change in daytime (respectively nighttime) SBP from baseline to Week 4 was predicted at the median baseline level. The change from baseline of daytime (respectively nighttime) SBP was calculated using the time weighted average of the AUC of DBP obtained over daytime (respectively nighttime)
In the analysis, if participants took prohibited antihypertensive treatment before Week 4, their subsequent measurements were excluded. In such cases, the excluded measurements were imputed by increasing the 24-hour SBP by 3 mmHg from the baseline value at Week 4. Moreover, participants who discontinued of study treatment due to any reason prior to the Week 4 were excluded from the analysis. The multiple imputation approach was used. Daytime: from 7am until 10 pm. Nighttime: from 10pm until 7 am.

End point type	Secondary

End point timeframe:

Baseline, Week 4

End point values	LOU064 (remibrutinib)			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: millimeter of mercury (mmHg)				
arithmetic mean (confidence interval 95%)				
daytime average SBP	-1.2 (-2.3 to -0.0)			
nighttime average SBP	-0.9 (-2.2 to 0.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated Mean Change from Baseline at Week 4 in daytime and nighttime average DBP measured by ABPM

End point title	Estimated Mean Change from Baseline at Week 4 in daytime and nighttime average DBP measured by ABPM

End point description:

The change in daytime (respectively nighttime) weighted average DBP was analyzed using linear regression model with baseline weighted average daytime DBP (respectively nighttime) as a covariate. The change in daytime (respectively nighttime) DBP from baseline to Week 4 was predicted at the median baseline level. The change from baseline of daytime (respectively nighttime) DBP was calculated using the time weighted average of the AUC of DBP obtained over daytime (respectively nighttime) In the analysis, if participants took prohibited antihypertensive treatment before Week 4, their subsequent measurements were excluded. In such cases, the excluded measurements were imputed by increasing the 24-hour DBP by 3 mmHg from the baseline value at Week 4. Moreover, participants who discontinued of study treatment due to any reason prior to the Week 4 were excluded from the analysis. The multiple imputation approach was used. Daytime: from 7am until 10 pm. Nighttime: from 10pm until 7 am.

End point type	Secondary

End point timeframe:

Baseline, Week 4

End point values	LOU064 (remibrutinib)			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: millimeter of mercury (mmHg)				
arithmetic mean (confidence interval 95%)				
daytime average DBP	-0.6 (-1.3 to 0.2)			
nighttime average DBP	0.2 (-0.8 to 1.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment adverse events and deaths were reported from first dose of study medication up to 28 days after last dose of study medication, assessed up to approximately 18 weeks.

Adverse event reporting additional description:

Consistent with EudraCTdisclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	LOU064 25mg b.i.d.

Reporting group description:

LOU064 25mg b.i.d.

Serious adverse events	LOU064 25mg b.i.d.		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 144 (2.78%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Aortic dissection			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Chronic spontaneous urticaria			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	LOU064 25mg b.i.d.		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 144 (22.22%)		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 144 (9.03%)		
occurrences (all)	14		
Skin and subcutaneous tissue disorders			
Chronic spontaneous urticaria			
subjects affected / exposed	8 / 144 (5.56%)		
occurrences (all)	10		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 144 (8.33%)		
occurrences (all)	13		

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