Clinical trial results:
A randomized, single dose, crossover study in healthy volunteers to investigate the relative bioavailability of linaprazan for a new oral tablet formulation of linaprazan glurate, and to assess the effect of food on the pharmacokinetics of linaprazan

Summary

EudraCT number	2022-002273-29
Trial protocol	SI
Global end of trial date	03 January 2023

Results information

Result version number	v1 (current)
This version publication date	30 May 2025
First version publication date	30 May 2025

Trial information

Trial identification

Sponsor protocol code	CX842A2106

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05627518
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cinclus Pharma Holding AB Publ.
Sponsor organisation address	World Trade Center, Kungsbron 1, Stockholm, Sweden, SE-111 22
Public contact	Gösta Hiller, Head of Project and Process Management, Cinclus Pharma Holding AB Publ., +46 723 72 59 58, gosta.hiller@cinclupharma.com
Scientific contact	Kajsa Larsson, CMO, Cinclus Pharma Holding AB Publ., +46 70 675 01 28, kajsa.larsson@cinclupharma.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	26 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 January 2023
Global end of trial reached?	Yes
Global end of trial date	03 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this single-dose, randomized, 3-way cross-over study are to evaluate the relative bioavailability of linaprazan between the new test formulation of linaprazan glurate and the previously studied reference formulation of linaprazan glurate after the administration of single 100 mg doses in fasting conditions and to assess the effect of a high-fat, high-calorie meal on the PK of linaprazan after the administration of single 100 mg doses of the test formulation.

Protection of trial subjects:

This study was conducted in compliance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use E6 (Revision 2) Section 3, Institutional Review Board/Independent Ethics Committee guidelines, Good Clinical Practice regulations and guidelines, and all applicable local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 November 2022
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	Slovenia: 67
Worldwide total number of subjects	67
EEA total number of subjects	67

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)	67
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 67 Subjects were enrolled in the study. All subject were randomized and recieved treatment. Of the 67 subjects, 49 completed all three arms of the study. The main reasons for discontinuation were protocol violations (12 subjects), adverse event (3 subjects), and withdrawal by subject (3 subjects)

Pre-assignment

Screening details:

Key eligibility criteria:
Medically healthy volunteers without clinically signifincant MedHis, aged 18-65, BMI 18.5-30.0 kg/m2
Adequate contraception or non-child bearing potential.

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	TREATMENT A, 4 x 25mg reference formulation, fasted

Arm description:

4 x 25 mg linaprazan glurate reference formulation in fasted condition

Arm type	Experimental
Investigational medicinal product name	4 x 25 mg linaprazan glurate reference formulation
Investigational medicinal product code	
Other name	CX842
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg (4 x 25mg) linaprazan glurate reference formulation

Arm title	TREATMENT B, 100 mg test formulation, fasted condition

Arm description:

1 x 100 mg linaprazan glurate test formulation in fasted condition

Arm type	Experimental
Investigational medicinal product name	100 mg linaprazan glurate test formulation
Investigational medicinal product code	
Other name	CX842
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 x 100 mg linaprazan glurate test formulation

Arm title	TREATMENT C, 100 mg test formulation, fed condition

Arm description:

1 x 100 mg linaprazan glurate test formulation in fed condition

Arm type	Experimental

Investigational medicinal product name	100 mg linaprazan glurate test formulation
Investigational medicinal product code	
Other name	CX842
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 x 100 mg linaprazan glurate test formulation

Arm title	Exploratory arm with underdosed subjects, 25 mg

Arm description:

Subjects who were underdosed at treatment A with 1 x 25 mg linaprazan glurate in fed condition. PK results will not be presented from this arm, but they are part of the Safeyt analysis set.

Arm type	Experimental
Investigational medicinal product name	1 x 25 mg linaprazan glurate reference formulation
Investigational medicinal product code	
Other name	CX842
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg (1 x 25mg) linaprazan glurate reference formulation - erroneously underdosed with one instead of 4 tablets. The data from this group were kept because it would have been unethical to not utilize it.

Number of subjects in period 1	TREATMENT A, 4 x 25mg reference formulation, fasted	TREATMENT B, 100 mg test formulation, fasted condition	TREATMENT C, 100 mg test formulation, fed condition
Started	67	53	50
Completed	51	49	49
Not completed	16	4	1
Consent withdrawn by subject	2	2	1
Adverse event, non-fatal	2	2	-
Protocol deviation	12	-	-

Number of subjects in period 1	Exploratory arm with underdosed subjects, 25 mg
Started	13
Completed	12
Not completed	1
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period

Reporting group description: -

Reporting group values	Treatment Period	Total	
Number of subjects	67	67	
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)	67	67	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	24.1		
standard deviation	± 6.07	-	
Gender categorical Units: Subjects			
Female	35	35	
Male	32	32	

Subject analysis sets

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All subject who were randomized, received at least one dose of linaprazan glurate, and who provided at least one post baseline assessment of data

Subject analysis set title	PK Analysis Set (PKAS)
Subject analysis set type	Per protocol

Subject analysis set description:

The PK analysis set (PKAS) consisted of all subjects who received at least 1 dose of linaprazan glurate and provided an evaluable plasma concentration profile, and who had no AEs or protocol deviations judged to affect the PK analysis

Reporting group values	Safety Analysis Set	PK Analysis Set (PKAS)	
Number of subjects	67	54	
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)	67	54	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	24.1	24.0	
standard deviation	± 6.07	± 6.54	
Gender categorical			
Units: Subjects			
Female	35	28	
Male	32	26	

End points

End points reporting groups

Reporting group title	TREATMENT A, 4 x 25mg reference formulation, fasted
Reporting group description:	
4 x 25 mg linaprazan glurate reference formulation in fasted condition	
Reporting group title	TREATMENT B, 100 mg test formulation, fasted condition
Reporting group description:	
1 x 100 mg linaprazan glurate test formulation in fasted condition	
Reporting group title	TREATMENT C, 100 mg test formulation, fed condition
Reporting group description:	
1 x 100 mg linaprazan glurate test formulation in fed condition	
Reporting group title	Exploratory arm with underdosed subjects, 25 mg
Reporting group description:	
Subjects who were underdosed at treatment A with 1 x 25 mg linaprazan glurate in fed condition. PK results will not be presented from this arm, but they are part of the Safeyt analysis set.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All subject who were randomized, received at least one dose of linaprazan glurate, and who provided at least one post baseline assessment of data	
Subject analysis set title	PK Analysis Set (PKAS)
Subject analysis set type	Per protocol
Subject analysis set description:	
The PK analysis set (PKAS) consisted of all subjects who received at least 1 dose of linaprazan glurate and provided an evaluable plasma concentration profile, and who had no AEs or protocol deviations judged to affect the PK analysis	

Primary: Relative Bioavailability of linaprazan, Test vs Reference formulation AUCinf

End point title	Relative Bioavailability of linaprazan, Test vs Reference formulation AUCinf[1]
End point description:	
Relative bioavailability of linaprazan, given linaprazan glurate test formulation vs. linaprazan glurate reference formulation. Cross-over.	
End point type	Primary
End point timeframe:	
Start to End of Study	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic results for the under-dosed group (Exploratory arm) will not be presented here, only per protocol groups. The exploratory arm is however represented in the Safety anaylsis set.

End point values	TREATMENT A, 4 x 25mg reference formulation, fasted	TREATMENT B, 100 mg test formulation, fasted condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	51		
Units: nanomole(s)/litre * h				
geometric mean (standard deviation)				
AUCinf	12341 (± 1.51)	25001 (± 1.32)		

Statistical analyses

Statistical analysis title	Ratio AUCinf Test vs Reference formulation

Statistical analysis description:

A comparison of natural-log (ln)-transformed PK parameters to evaluate the relative bioavailability of Test vs. Reference, by a linear fixed effects model analysis using PROC MIXED of SAS® incl SEQUENCE, TREATMENT, PERIOD and SUBJECT as fixed effects, with SUBJECT nested within SEQUENCE. The inferential results (least-squares [LS] means, diff. between LS means, and 90% CIs of the diff.) were exponentiated to the original scale. Geometric LS means, geometric mean ratios and 90% CIs are presented.

Comparison groups	TREATMENT A, 4 x 25mg reference formulation, fasted v TREATMENT B, 100 mg test formulation, fasted condition
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Geometric mean LS ratio
Point estimate	1.9954
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.8399
upper limit	2.1641

Notes:

[2] - Due to limitations in the system, the "subjects in this analysis" figure given is incorrect as this is a cross-over study. For the true numbers, please see the "Subjects analysed" in the Reporting Groups.

The Ratio between the comparison groups were as follows: Treatment B/Treatment A

Primary: Relative Bioavailability of linaprazan, Test vs Reference Cmax

End point title	Relative Bioavailability of linaprazan, Test vs Reference Cmax[3]

End point description:

Ratio of linaprazan Cmax comparing Treatment A, linaprazan glurate test formulation 1 x 100 mg test formulaiton vs Treatment B, 4 x 25 mg reference formulation, in fed condition.

End point type	Primary

End point timeframe:

From study start to study end

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetic results for the under-dosed group (Exploratory arm) will not be presented here, only per protocol groups. The exploratory arm is however represented in the Safety anaylsis set.

End point values	TREATMENT A, 4 x 25mg reference formulation, fasted	TREATMENT B, 100 mg test formulation, fasted condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	53		
Units: nanomole(s)/litre				
geometric mean (standard deviation)				
Cmax	1430.0 (± 1.83)	3462.2 (± 1.25)		

Statistical analyses

Statistical analysis title	Ratio Cmax Test vs Reference formulation

Statistical analysis description:

A comparison of natural-log (ln)-transformed PK parameters to evaluate the relative bioavailability of Test vs. Reference, by a linear fixed effects model analysis using PROC MIXED of SAS® incl SEQUENCE, TREATMENT, PERIOD and SUBJECT as fixed effects, with SUBJECT nested within SEQUENCE. The inferential results (least-squares [LS] means, diff. between LS means, and 90% CIs of the diff.) were exponentiated to the original scale. Geometric LS means, geometric mean ratios and 90% CIs are presented.

Comparison groups	TREATMENT B, 100 mg test formulation, fasted condition v TREATMENT A, 4 x 25mg reference formulation, fasted
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	other[4]
Method	Mixed models analysis
Parameter estimate	Geometric mean LS ratio
Point estimate	2.3167
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.0922
upper limit	2.5652

Notes:

[4] - Due to limitations in the system, the "subjects in this analysis" figure given is incorrect as this is a cross-over study. For the true numbers, please see the "Subjects analysed" in the Reporting Groups.

The Ratio between the comparison groups were as follows: Treatment B/Treatment A

Primary: Relative Bioavailability of linaprazan, Fed vs Fasted AUCinf

End point title	Relative Bioavailability of linaprazan, Fed vs Fasted AUCinf[5]

End point description:

Relative bioavailability of linaprazan, given linaprazan glurate test formulation under fed or fasting conditions. Cross-over.

End point type	Primary

End point timeframe:

Start to end of study

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic results for the under-dosed group (Exploratory arm) will not be presented here, only per protocol groups. The exploratory arm is however represented in the Safety anaylsis set.

End point values	TREATMENT B, 100 mg test formulation, fasted condition	TREATMENT C, 100 mg test formulation, fed condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	49		
Units: nanomole(s)/litre * h				
geometric mean (standard deviation)				
AUCinf	25001 (± 1.32)	19448.9 (± 1.32)		

Statistical analyses

Statistical analysis title	Ratio AUCinf Fed vs Fasted

Statistical analysis description:

A comparison of natural-log (ln)-transformed PK parameters to evaluate the relative bioavailability of Test vs. Reference, by a linear fixed effects model analysis using PROC MIXED of SAS® incl SEQUENCE, TREATMENT, PERIOD and SUBJECT as fixed effects, with SUBJECT nested within SEQUENCE. The inferential results (least-squares [LS] means, diff. between LS means, and 90% CIs of the diff.) were exponentiated to the original scale. Geometric LS means, geometric mean ratios and 90% CIs are presented.

Comparison groups	TREATMENT B, 100 mg test formulation, fasted condition v TREATMENT C, 100 mg test formulation, fed condition
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Geometric mean LS ratio
Point estimate	0.757
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7009
upper limit	0.8177

Notes:

[6] - Due to limitations in the system, the "subjects in this analysis" figure given is incorrect as this is a cross-over study. For the true numbers, please see the "Subjects analysed" in the Reporting Groups.

The Ratio between the comparison groups were as follows: Treatment C/Treatment B

Primary: Relative Bioavailability of linaprazan, Fed vs Fasted Cmax

End point title	Relative Bioavailability of linaprazan, Fed vs Fasted Cmax[7]

End point description:

End point type	Primary

End point timeframe:

Start to end of study

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetic results for the under-dosed group (Exploratory arm) will not be presented here, only per protocol groups. The exploratory arm is however represented in the Safety anaylsis set.

End point values	TREATMENT B, 100 mg test formulation, fasted condition	TREATMENT C, 100 mg test formulation, fed condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	50		
Units: nanomole(s)/litre				
geometric mean (standard deviation)	3462.2 (± 1.25)	1608.2 (± 1.29)		

Statistical analyses

Statistical analysis title	Ratio Cmax Fed vs Fasted

Statistical analysis description:

A comparison of natural-log (ln)-transformed PK parameters to evaluate the food effect by a linear fixed effects model analysis using PROC MIXED of SAS® including SEQUENCE, TREATMENT, PERIOD and SUBJECT as fixed effects, with SUBJECT nested within SEQUENCE. The inferential results (least-squares [LS] means, diff. between LS means, and 90% CIs of the diff.) were exponentiated to the original scale. Geometric LS means, geometric mean ratios and 90% CIs are presented.

Comparison groups	TREATMENT B, 100 mg test formulation, fasted condition v TREATMENT C, 100 mg test formulation, fed condition
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Geometric mean LS ratio
Point estimate	0.454
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.4094
upper limit	0.5035

Notes:

[8] - Due to limitations in the system, the "subjects in this analysis" figure given is incorrect as this is a cross-over study. For the true numbers, please see the "Subjects analysed" in the Reporting Groups.

The Ratio between the comparison groups were as follows: Treatment C/Treatment B

Primary: Relative Bioavailability of linaprazan, Test vs Reference formulation AUClast

End point title	Relative Bioavailability of linaprazan, Test vs Reference formulation AUClast[9]

End point description:

Relative bioavailability of linaprazan, given linaprazan glurate test formulation vs. linaprazan glurate reference formulation. Cross-over.

End point type	Primary

End point timeframe:

Start to End of Study

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic results for the under-dosed group (Exploratory arm) will not be presented here, only per protocol groups. The exploratory arm is however represented in the Safety anaylsis set.

End point values	TREATMENT A, 4 x 25mg reference formulation, fasted	TREATMENT B, 100 mg test formulation, fasted condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	53		
Units: nanomole(s)/Litre * h				
geometric mean (standard deviation)				
AUClast	10016.2 (± 2.78)	24175.8 (± 1.34)		

Statistical analyses

Statistical analysis title	Ratio AUClast Test vs Reference formulation

Statistical analysis description:

A comparison of natural-log (ln)-transformed PK parameters to evaluate the relative bioavailability of Test vs. Reference, by a linear fixed effects model analysis using PROC MIXED of SAS® incl SEQUENCE, TREATMENT, PERIOD and SUBJECT as fixed effects, with SUBJECT nested within SEQUENCE. The inferential results (least-squares [LS] means, diff. between LS means, and 90% CIs of the diff.) were exponentiated to the original scale. Geometric LS means, geometric mean ratios and 90% CIs are presented.

Comparison groups	TREATMENT A, 4 x 25mg reference formulation, fasted v TREATMENT B, 100 mg test formulation, fasted condition
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Ratio
Point estimate	2.125
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.9664
upper limit	2.2963

Notes:

[10] - Due to limitations in the system, the "subjects in this analysis" figure given is incorrect as this is a cross-over study. For the true numbers, please see the "Subjects analysed" in the Reporting Groups.

The Ratio between the comparison groups were as follows: Treatment B/Treatment A

Primary: Relative Bioavailability of linaprazan, Fed vs Fasted AUClast

End point title	Relative Bioavailability of linaprazan, Fed vs Fasted AUClast[11]

End point description:

Relative bioavailability of linaprazan, given linaprazan glurate test formulation under fed or fasting conditions. Cross-over.

End point type	Primary

End point timeframe:

Start to end of study

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic results for the under-dosed group (Exploratory arm) will not be presented

here, only per protocol groups. The exploratory arm is however represented in the Safety anaylsis set.

End point values	TREATMENT B, 100 mg test formulation, fasted condition	TREATMENT C, 100 mg test formulation, fed condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	50		
Units: nanomole(s)/Litre * h				
geometric mean (standard deviation)				
AUClast	24175.8 (± 1.34)	19022.8 (± 1.32)		

Statistical analyses

Statistical analysis title	Ratio AUClast Fed vs Fasted

Statistical analysis description:

A comparison of natural-log (ln)-transformed PK parameters to evaluate the relative bioavailability of Test vs. Reference, by a linear fixed effects model analysis using PROC MIXED of SAS® incl SEQUENCE, TREATMENT, PERIOD and SUBJECT as fixed effects, with SUBJECT nested within SEQUENCE. The inferential results (least-squares [LS] means, diff. between LS means, and 90% CIs of the diff.) were exponentiated to the original scale. Geometric LS means, geometric mean ratios and 90% CIs are presented.

Comparison groups	TREATMENT C, 100 mg test formulation, fed condition v TREATMENT B, 100 mg test formulation, fasted condition
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Geometric mean LS ratio
Point estimate	0.7684
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7102
upper limit	0.8313

Notes:

[12] - Due to limitations in the system, the "subjects in this analysis" figure given is incorrect as this is a cross-over study. For the true numbers, please see the "Subjects analysed" in the Reporting Groups.

The Ratio between the comparison groups were as follows: Treatment C/Treatment B

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for reporting is from time of being randomized until end of study.

Adverse event reporting additional description:

During the study period, a total of 35 subjects experienced at least one TEAE for a total of 55 events. A total of 2 events, were considered by the Investigator as possibly related to study treatment. 1 event of Gastrointestinal disorder (Constipation) and 1 event of liver disorder (Mild hepatopathy). Overall there was 1 SAE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	TEAE

Reporting group description:

During the overall study period, 35 subjects (52.2%) experienced at least one TEAE for a total of 55 events. The most commonly reported TEAEs by MedDRA PTs were nasopharyngitis (7 subjects [10.4%]) and tachycardia (7 subjects [10.4%]), followed by headache (5 subjects [7.5%]), hypertension (3 subjects [4.5%]), phlebitis (3 subjects [4.5%]) and constipation (3 subjects [4.5%]). The TEAEs Papule, Blood Pressure Diastolic increased, Rhinitis, Diarrhea and Vomiting all occurred in 2 subjects (3%) each. All other TEAEs were unique events reported in single subjects.

Serious adverse events	TEAE		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 67 (1.49%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Skin and subcutaneous tissue disorders			
Skin bacterial infection	Additional description: The subject experienced a TEAE of phlebitis (verebatim: phlebitis of the left cubital vein after i.v. cannula post insertion). The PI considered event to be moderate, unlikely related to the IP, but possibly related to the study procedures.		
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 4.5 %

Non-serious adverse events	TEAE		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 67 (52.24%)		

Investigations Blood pressure diastolic decreased subjects affected / exposed occurrences (all)	 2 / 67 (2.99%) 2		
Vascular disorders Hypertension subjects affected / exposed occurrences (all) Phlebitis subjects affected / exposed occurrences (all)	 3 / 67 (4.48%) 3 3 / 67 (4.48%) 3		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	 7 / 67 (10.45%) 8		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	 5 / 67 (7.46%) 6 1 / 67 (1.49%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 2 / 67 (2.99%) 2 2 / 67 (2.99%) 2 3 / 67 (4.48%) 4		
Skin and subcutaneous tissue disorders Papule subjects affected / exposed occurrences (all)	 2 / 67 (2.99%) 2		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	9 / 67 (13.43%) 10		
Rhinitis subjects affected / exposed occurrences (all)	2 / 67 (2.99%) 2		

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