Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of SNF472 When added to Background Care for the Treatment of Calciphylaxis.

Summary

EudraCT number	2018-001301-90
Trial protocol	GB ES PL BE IT
Global end of trial date	24 October 2022

Results information

Result version number	v1
This version publication date	30 November 2023
First version publication date	30 November 2023

Trial information

Trial identification

Sponsor protocol code	SNFCT2017-06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04195906
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanifit Therapeutics S.A., A CSL Vifor Pharma Company
Sponsor organisation address	PARC BIT. Europa Building. 2nd floor, Palma, Spain, 07121
Public contact	Peter Szecsödy, Sanifit Therapeutics S.A , +41 588529079, peter.szecsoedy@viforpharma.com
Scientific contact	Peter Szecsödy, Sanifit Therapeutics S.A , +41 588529079, peter.szecsoedy@viforpharma.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	12 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 October 2022
Global end of trial reached?	Yes
Global end of trial date	24 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of SNF472 compared with placebo when added to background care for the treatment of calciphylaxis.
To evaluate the safety and tolerability of SNF472 compared with placebo when added to background care for the treatment of calciphylaxis.

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki including amendments in force up to and including the time the study was conducted. The study was conducted in compliance with the International Council for Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP), Committee for Proprietary Medicinal Products Guideline (CPMP/ICH/135/95), compliant with the EU Clinical Trial Directive (Directive 2001/20/EC) and/or the Code of Federal Regulations (CFR) for informed consent and protection of subject rights (21 CFR, Parts 50 and 56), and in accordance with United States Food and Drug Administration (US FDA) regulations.

A data and safety monitoring board (DSMB) was established and was responsible for safeguarding the interests of trial participants and assessing the safety of the interventions during the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 December 2019
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	Poland: 3
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	United States: 64
Worldwide total number of subjects	71
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	54
From 65 to 84 years	16
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 148 participants were screened in 48 sites in 5 countries; 77 participants were not enrolled because
they were screen failures (did not meet eligibility criteria). A total of 71 participants were randomized in the
study to receive SNF472 or placebo.

Period 1

Period 1 title	Part 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Part 1 was performed in a double-blind manner.
The Investigator, site staff, subjects, and Sponsor staff (including designees) involved in the conduct of the study and data management remained blinded to the treatment assignment for Part 1 for the duration of the study including Part 2 and follow-up until the study database lock, except if unblinding was required.

Arms

Are arms mutually exclusive?	Yes
Arm title	SNF472

Arm description:

Part 1 (double-blind period):
Participants received SNF472 for 12 weeks in addition to their background care.

Arm type	Experimental
Investigational medicinal product name	SNF472
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: 7 mg/kg SNF472 diluted in 100 mL physiological saline. Administered 3 times weekly by intravenous
infusion through the hemodialysis machine in conjunction with the subject's hemodialysis sessions for 12 weeks.

Arm title	Placebo

Arm description:

Part 1 (double-blind period)
Participants received placebo for 12 weeks in addition to their background care.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: Matching placebo (saline) diluted in 100 mL physiological saline. Administered 3 times weekly by intravenous infusion through the hemodialysis machine in conjunction with the subject's hemodialysis

sessions
fo 12 weeks

Number of subjects in period 1	SNF472	Placebo
Started	37	34
Completed	34	26
Not completed	3	8
Consent withdrawn by subject	-	1
Adverse event, non-fatal	3	7

Period 2

Period 2 title	Part 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Open-label treatment period

Arms

Are arms mutually exclusive?	Yes
Arm title	SNF472

Arm description:

Part 2 (Open-label):
Participants received SNF472 for 12 weeks in addition to their background care.

Arm type	Experimental
Investigational medicinal product name	SNF472
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: 7 mg/kg SNF472 diluted in 100 mL physiological saline. Administered 3 times weekly by intravenous
infusion through the hemodialysis machine in conjunction with the subject's hemodialysis sessions for 12 weeks.

Arm title	Placebo

Arm description:

Part 2 (Open-label):
Participants received SNF472 for 12 weeks in addition to their background care.

Arm type	Experimental
Investigational medicinal product name	SNF472
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: 7 mg/kg SNF472 diluted in 100 mL physiological saline. Administered 3 times weekly by intravenous
infusion through the hemodialysis machine in conjunction with the subject's hemodialysis sessions for 12 weeks.

Number of subjects in period 2	SNF472	Placebo
Started	34	26
Completed	32	19
Not completed	2	7
Consent withdrawn by subject	-	3
Adverse event, non-fatal	1	1
Other	1	3

Baseline characteristics

Reporting groups	
Reporting group title	SNF472
Reporting group description:	
Part 1 (double-blind period): Participants received SNF472 for 12 weeks in addition to their background care.	
Reporting group title	Placebo
Reporting group description:	
Part 1 (double-blind period) Participants received placebo for 12 weeks in addition to their background care.	

Reporting group values	SNF472	Placebo	Total
Number of subjects	37	34	71
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	27	27	54
>=65 years	10	7	17
Gender categorical Units: Subjects			
Female	23	21	44
Male	14	13	27

End points

End points reporting groups

Reporting group title	SNF472
Reporting group description:	
Part 1 (double-blind period): Participants received SNF472 for 12 weeks in addition to their background care.	
Reporting group title	Placebo
Reporting group description:	
Part 1 (double-blind period) Participants received placebo for 12 weeks in addition to their background care.	
Reporting group title	SNF472
Reporting group description:	
Part 2 (Open-label): Participants received SNF472 for 12 weeks in addition to their background care.	
Reporting group title	Placebo
Reporting group description:	
Part 2 (Open-label): Participants received SNF472 for 12 weeks in addition to their background care.	

Primary: Absolute Change in the BWAT - CUA Score for the Primary Lesion

End point title	Absolute Change in the BWAT - CUA Score for the Primary Lesion
End point description:	
The Bates Jensen Wound Assessment Tool (BWAT) CUA score ranges from a minimum score of 8 (best) to a maximum score of 40 (worst). BWAT-CUA= Bates-Jensen Wound Assessment Tool-Calcific Uremic Arteriolopathy	
End point type	Primary
End point timeframe:	
from Baseline to Week 12	

End point values	SNF472	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	34		
Units: score on a scale				
arithmetic mean (standard deviation)	-5.3 (± 5.18)	-6.0 (± 6.17)		

Statistical analyses

Statistical analysis title	Mixed model for repeated measures

Statistical analysis description:

The MMRM model includes fixed effect terms for randomized treatment, visit, baseline sodium thiosulfate use, baseline BWAT-CUA score and visit by randomized treatment interaction. Participant is fitted as random effect and an
unstructured variance-covariance matrix is used.

Comparison groups	SNF472 v Placebo
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.877
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	0.27
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	-2.46
upper limit	3
Variability estimate	Standard error of the mean
Dispersion value	1.328

Secondary: Absolute Change in Pain Visual Analog Score

End point title	Absolute Change in Pain Visual Analog Score

End point description:

The Pain Visual Analog Scale (VAS) score ranges from a minimum score of 0 (no pain) to 100 (worst possible pain).

End point type	Secondary

End point timeframe:

from Baseline to Week 12

End point values	SNF472	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	34		
Units: score on a scale				
arithmetic mean (standard deviation)	-19.5 (± 26.89)	-32.2 (± 38.53)		

Statistical analyses

Statistical analysis title	Mixed model for repeated measures

Statistical analysis description:

The MMRM model includes fixed effect terms for randomized treatment, visit, baseline sodium thiosulfate use, baseline BWAT-CUA score and visit by randomized treatment interaction. Participant is fitted as random effect and an unstructured variance-covariance matrix is used.

Comparison groups	Placebo v SNF472

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.146
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	11.49
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	-4.8
upper limit	27.78
Variability estimate	Standard error of the mean
Dispersion value	7.93

Secondary: Absolute Change in the Wound-Quality of Life Score

End point title	Absolute Change in the Wound-Quality of Life Score

End point description:

The Wound Quality of Life scale is a validated self-assessment tool that has been shown to be feasible for assessing health-related quality of life in patients with chronic wounds. Lower scores are associated with a better quality of life as reported by the patient.

End point type	Secondary

End point timeframe:

from Baseline to Week 12

End point values	SNF472	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	34		
Units: score on a scale				
arithmetic mean (standard deviation)	-0.67 (± 0.798)	-0.74 (± 1.175)		

Statistical analyses

Statistical analysis title	Mixed model for repeated measures

Statistical analysis description:

The MMRM model includes fixed effect terms for randomized treatment, visit, baseline sodium thiosulfate use, baseline BWAT-CUA score and visit by randomized treatment interaction. Participant is fitted as random effect and an unstructured variance-covariance matrix is used.

Comparison groups	SNF472 v Placebo

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.706
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	0.09
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	-0.38
upper limit	0.56
Variability estimate	Standard error of the mean
Dispersion value	0.237

Secondary: Absolute Change in the BWAT Total Score for the Primary Lesion

End point title	Absolute Change in the BWAT Total Score for the Primary Lesion

End point description:

The Bates Jensen Wound Assessment Tool (BWAT) score ranges from a minimum score of 9 (best) to a maximum score of 65 (worst) score.

End point type	Secondary

End point timeframe:

from Baseline to Week 12

End point values	SNF472	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	34		
Units: score on a scale				
arithmetic mean (standard deviation)	-11.0 (± 9.85)	-11.7 (± 12.23)		

Statistical analyses

Statistical analysis title	Mixed model for repeated measures

Statistical analysis description:

The MMRM model includes fixed effect terms for randomized treatment, visit, baseline sodium thiosulfate use, baseline BWAT-CUA score and visit by randomized treatment interaction. Participant is fitted as random effect and an unstructured variance-covariance matrix is used.

Comparison groups	SNF472 v Placebo

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.995
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.02
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	-5.27
upper limit	5.24
Variability estimate	Standard error of the mean
Dispersion value	2.63

Secondary: Qualitative Wound Image Evaluation for the Primary Lesion

End point title	Qualitative Wound Image Evaluation for the Primary Lesion

End point description:

A qualitative assessment (Worsened, Equal to, or Improved Relative to Baseline) was assigned

End point type	Secondary

End point timeframe:

at Week 12

End point values	SNF472	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	34		
Units: Count of Participants				
Worsened	6	7		
Equal	0	1		
Improved	23	18		
Missing	8	8		

Statistical analyses

Statistical analysis title	Logistic regression odds ratio

Statistical analysis description:

This model includes the stratification factor sodium thiosulfate use at baseline and the treatment as covariates. As there is only a measure post-baseline, a logistic regression model was run instead of a generalized estimating equations model.

The odds ratio displayed is the odds ratio of having an improved result of SNF472 versus Placebo. The results 'Worsened', 'Equal', and 'Missing' are combined in one category and it is the reference for the odds ratio calculation.

Comparison groups	SNF472 v Placebo

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.384
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	4.09
Variability estimate	Standard error of the mean
Dispersion value	0.498

Secondary: Rate of Change in Opioid Use as Measured in Morphine Milligram Equivalents (MME)

End point title	Rate of Change in Opioid Use as Measured in Morphine Milligram Equivalents (MME)
End point description:	
Change from baseline in opioid use MME = Morphine Milligram Equivalents	
End point type	Secondary
End point timeframe:	
from Baseline to Week 12	

End point values	SNF472	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	34		
Units: MME/week				
least squares mean (standard error)	0.46 (± 0.461)	-0.11 (± 0.499)		

Statistical analyses

Statistical analysis title	Mixed model for repeated measures

Statistical analysis description:

The MMRM model includes fixed effect terms for randomized treatment, continuous variables maintenance opioid dose, Week (1 to 12) and Week by randomized treatment interaction. The random coefficients are the intercept and Week as a continuous variable.

Comparison groups	SNF472 v Placebo

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.406
Method	Mixed models analysis
Parameter estimate	Difference in slopes between arms
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	1.93
Variability estimate	Standard error of the mean
Dispersion value	0.68

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part 1: 12-week double-blind, randomized, placebo-controlled treatment period
Part 2: 12-week open-label treatment period after completion of part 1 period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	SNF472 - Safety Analysis Population (Part 1)

Reporting group description:

Participants who received SNF472 treatment during part 1 (Double-blind Period).

Reporting group title	Placebo - Safety Analysis Population (Part 1)

Reporting group description:

Participants who received placebo during part 1 (Double-blind Period).

Reporting group title	SNF472 Open label - Safety Analysis Population (Part 2)

Reporting group description:

Participants who received SNF472 treatment during part 2 (Open-label)

Serious adverse events	SNF472 - Safety Analysis Population (Part 1)	Placebo - Safety Analysis Population (Part 1)	SNF472 Open label - Safety Analysis Population (Part 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 38 (34.21%)	17 / 33 (51.52%)	18 / 60 (30.00%)
number of deaths (all causes)	1	6	1
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extremity necrosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Subclavian vein thrombosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive urgency			
subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 38 (2.63%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous graft site haemorrhage			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula thrombosis			

subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 38 (2.63%)	2 / 33 (6.06%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Cardiac failure			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			

subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood loss anaemia			

subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dieulafoy's vascular malformation			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
End stage renal disease			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arteriovenous fistula site infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 38 (2.63%)	3 / 33 (9.09%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 38 (2.63%)	1 / 33 (3.03%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	1 / 38 (2.63%)	2 / 33 (6.06%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 38 (2.63%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			

subjects affected / exposed	0 / 38 (0.00%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Calciphylaxis			
subjects affected / exposed	2 / 38 (5.26%)	5 / 33 (15.15%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypervolaemia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lactic acidosis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	SNF472 - Safety Analysis Population (Part 1)	Placebo - Safety Analysis Population (Part 1)	SNF472 Open label - Safety Analysis Population (Part 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 38 (71.05%)	21 / 33 (63.64%)	33 / 60 (55.00%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 38 (7.89%)	1 / 33 (3.03%)	5 / 60 (8.33%)
occurrences (all)	3	2	5
Arteriovenous fistula site complication			
subjects affected / exposed	2 / 38 (5.26%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences (all)	2	0	1
Arteriovenous fistula site haemorrhage			
subjects affected / exposed	2 / 38 (5.26%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences (all)	2	0	1
Vascular access malfunction			

subjects affected / exposed	0 / 38 (0.00%)	2 / 33 (6.06%)	2 / 60 (3.33%)
occurrences (all)	0	2	2
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 38 (0.00%)	2 / 33 (6.06%)	3 / 60 (5.00%)
occurrences (all)	0	2	3
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 38 (5.26%)	1 / 33 (3.03%)	1 / 60 (1.67%)
occurrences (all)	5	1	1
Ventricular tachycardia			
subjects affected / exposed	0 / 38 (0.00%)	2 / 33 (6.06%)	0 / 60 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 38 (7.89%)	3 / 33 (9.09%)	0 / 60 (0.00%)
occurrences (all)	3	5	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	2 / 38 (5.26%)	2 / 33 (6.06%)	3 / 60 (5.00%)
occurrences (all)	2	2	4
Pyrexia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences (all)	2	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 33 (0.00%)	2 / 60 (3.33%)
occurrences (all)	2	0	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 38 (5.26%)	4 / 33 (12.12%)	3 / 60 (5.00%)
occurrences (all)	2	4	3
Vomiting			
subjects affected / exposed	5 / 38 (13.16%)	1 / 33 (3.03%)	2 / 60 (3.33%)
occurrences (all)	6	1	2
Diarrhoea			

subjects affected / exposed	2 / 38 (5.26%)	1 / 33 (3.03%)	5 / 60 (8.33%)
occurrences (all)	2	1	5
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 38 (0.00%)	2 / 33 (6.06%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 38 (0.00%)	2 / 33 (6.06%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	4 / 38 (10.53%)	2 / 33 (6.06%)	5 / 60 (8.33%)
occurrences (all)	4	2	5
Arthralgia			
subjects affected / exposed	5 / 38 (13.16%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences (all)	6	0	1
Back pain			
subjects affected / exposed	2 / 38 (5.26%)	0 / 33 (0.00%)	2 / 60 (3.33%)
occurrences (all)	2	0	2
Muscular weakness			
subjects affected / exposed	2 / 38 (5.26%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 38 (2.63%)	2 / 33 (6.06%)	1 / 60 (1.67%)
occurrences (all)	1	2	1
Cellulitis			
subjects affected / exposed	2 / 38 (5.26%)	1 / 33 (3.03%)	0 / 60 (0.00%)
occurrences (all)	2	1	0
Metabolism and nutrition disorders			
Calciphylaxis			
subjects affected / exposed	8 / 38 (21.05%)	8 / 33 (24.24%)	4 / 60 (6.67%)
occurrences (all)	9	9	8
Decreased appetite			

subjects affected / exposed	2 / 38 (5.26%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 38 (2.63%)	1 / 33 (3.03%)	4 / 60 (6.67%)
occurrences (all)	1	1	4
Hypervolaemia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 33 (0.00%)	1 / 60 (1.67%)
occurrences (all)	2	0	1
Hypokalaemia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 33 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2019	Protocol Amendment 1
21 May 2021	Protocol Amendment 2
09 December 2021	Protocol Amendment 3

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported