Clinical trial results:
An adaptive open label, multiple ascending dose study of the safety, tolerability and bio-effect of Aurase for wound debridement in patients with venous leg ulcers and diabetic foot ulcers (CLEANVLU/DFU)

Summary

EudraCT number	2020-001392-32
Trial protocol	HU
Global end of trial date	06 February 2023

Results information

Result version number	v1 (current)
This version publication date	13 March 2024
First version publication date	13 March 2024

Trial information

Trial identification

Sponsor protocol code	SC-VLU-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04956900
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	SolasCure Ltd
Sponsor organisation address	Wellington House, East Road, Cambridge, United Kingdom, CB1 1BH
Public contact	David Fairlamb, SolasCure Limited, 44 1274519914, dfairlamb@solascure.com
Scientific contact	David Fairlamb, SolasCure Limited, 44 1274519914, dfairlamb@solascure.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	01 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 February 2023
Global end of trial reached?	Yes
Global end of trial date	06 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of multiple ascending doses of Aurase Wound Gel when administered cutaneously (topically) to participants with Venous Leg Ulcers (VLU)

Protection of trial subjects:

Study will be conducted in accordance with the requirements of International Council for Harmonisation Good Clinical Practice (ICH GCP), the Declaration
of Helsinki (revised version of 2013), Good Manufacturing Practice (GMP), and the current national regulations and guidelines. The protocol will be approved by both the local ethics committee(s) (IEC) / institutional review board(s) (IRB) and regulatory authority(ices).

Safety was evaluated based on adverse events (AEs), clinical laboratory tests, tolerability assessments, ECGs, concomitant medication review as well as a number of entry assessments (e.g. vital signs, medical history, physical examination)

For each study cohort a sentinel patient was enrolled and safety data through at least day 8 was reviewed in a safety review meeting (sponsor and enrolling investigator attended). A safety review meeting was also conducted at the end of each cohort to determine whether it was safe to dose escalate in the next cohort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 October 2021
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	United Kingdom: 1
Country: Number of subjects enrolled	Hungary: 27
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	43
EEA total number of subjects	27

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)	16
From 65 to 84 years	25
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

A total of 43 participants were enrolled onto the study and received treatment however 1 participant number has been excluded from demographic summary data as they were re-screened with a different reference ulcer

Pre-assignment

Screening details:

Participants with at least one defined VLU suitable for treatment that was no smaller than 2 cm2 but no larger than 50cm2 and was confirmed as venous in origin by clinical assessments, by Ankle Brachial Pressure Index (ABPI) ≥ 0.8 and/or toe systolic BP pressure > 70mm Hg and with presence of devitalized tissue suitable for debridement

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1; Aurase wound gel x0 dose concentration

Arm description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Arm type	Experimental
Investigational medicinal product name	Aurase Wound Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

Aurase wound gel x0 dose concentration administered cutaneously (topically) to the reference Venous Leg Ulcer (VLU) 3 times per week for up to 4 weeks. The actual volume of gel to be administered in the clinical trial will be dependent on the surface area of the VLU measured.

Arm title	Cohort 2; Aurase wound gel x1 dose concentration

Arm description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Arm type	Experimental
Investigational medicinal product name	Aurase Wound Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

Aurase wound gel x1 dose concentration administered cutaneously (topically) to the reference Venous Leg Ulcer (VLU) 3 times per week for up to 4 weeks. The actual volume of gel to be administered in the clinical trial will be dependent on the surface area of the VLU measured.

Arm title	Cohort 3; Aurase wound gel x1.8 dose concentration

Arm description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Arm type	Experimental
Investigational medicinal product name	Aurase Wound Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

Aurase wound gel x1.8 dose concentration administered cutaneously (topically) to the reference Venous Leg Ulcer (VLU) 3 times per week for up to 4 weeks. The actual volume of gel to be administered in the clinical trial will be dependent on the surface area of the VLU measured.

Arm title	Cohort 4; Aurase wound gel x5 dose concentration

Arm description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Arm type	Experimental
Investigational medicinal product name	Aurase Wound Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

Aurase wound gel x5 dose concentration administered cutaneously (topically) to the reference Venous Leg Ulcer (VLU) 3 times per week for up to 4 weeks. The actual volume of gel to be administered in the clinical trial will be dependent on the surface area of the VLU measured.

Arm title	Cohort 5; Aurase wound gel x9 dose concentration

Arm description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Arm type	Experimental
Investigational medicinal product name	Aurase Wound Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

Aurase wound gel x9 dose concentration administered cutaneously (topically) to the reference Venous Leg Ulcer (VLU) 3 times per week for up to 4 weeks. The actual volume of gel to be administered in the clinical trial will be dependent on the surface area of the VLU measured.

Number of subjects in period 1	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration
Started	5	9	10
Completed	5	7	10
Not completed	0	2	0
Adverse event, serious fatal	-	-	-
Adverse event, non-fatal	-	-	-
Protocol deviation	-	2	-

Number of subjects in period 1	Cohort 4; Aurase wound gel x5 dose concentration	Cohort 5; Aurase wound gel x9 dose concentration
Started	9	10
Completed	7	10
Not completed	2	0
Adverse event, serious fatal	1	-
Adverse event, non-fatal	1	-
Protocol deviation	-	-

Baseline characteristics

Reporting groups

Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	43	43	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	68.6		
standard deviation	± 14.8	-	
Gender categorical Units: Subjects			
Female	18	18	
Male	25	25	

Subject analysis sets

Subject analysis set title	Demographics set
Subject analysis set type	Full analysis

Subject analysis set description:

1 participant number has been excluded from demographic summary data as they were re-screened with a different reference ulcer

Subject analysis set title	Intent to treat population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intent to treat population consists of participants who are enrolled, receive at least one dose of study treatment, and have at least one assessment of safety and/ or tolerability.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population consists of all participants who take at least one administration of study treatment

Reporting group values	Demographics set	Intent to treat population	Safety population
Number of subjects	43	43	43
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	68.6		
standard deviation	± 14.75	±	±
Gender categorical Units: Subjects			
Female	18		
Male	24		

End points

End points reporting groups

Reporting group title	Cohort 1; Aurase wound gel x0 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Reporting group title	Cohort 2; Aurase wound gel x1 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Reporting group title	Cohort 3; Aurase wound gel x1.8 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Reporting group title	Cohort 4; Aurase wound gel x5 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Reporting group title	Cohort 5; Aurase wound gel x9 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Subject analysis set title	Demographics set
Subject analysis set type	Full analysis

Subject analysis set description:

1 participant number has been excluded from demographic summary data as they were re-screened with a different reference ulcer

Subject analysis set title	Intent to treat population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intent to treat population consists of participants who are enrolled, receive at least one dose of study treatment, and have at least one assessment of safety and/ or tolerability.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population consists of all participants who take at least one administration of study treatment

Primary: Change in Study Wound Pain Burden From Baseline Measured by Numerical Rating Scale (NRS) at Day 29 (End of Study)

End point title	Change in Study Wound Pain Burden From Baseline Measured by Numerical Rating Scale (NRS) at Day 29 (End of Study)[1]

End point description:

Subject will be asked to describe the level of wound pain on a scale of 0-10: 0 being no pain, 10 being worst imaginable pain. Baseline is defined as the last non-missing value (including scheduled and unscheduled assessments) prior to the participant receiving the first study treatment

End point type	Primary

End point timeframe:

Pre-dose at day 1 (baseline) through to day 29 (end of study)

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: Descriptive statistics only were used in the first-in-human clinical study

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	2.40 (± 1.52)	3.11 (± 1.05)	3.40 (± 1.51)	3.11 (± 2.71)
Day 29	1.00 (± 1.71)	2.22 (± 1.56)	2.50 (± 2.51)	2.13 (± 2.75)

End point values	Cohort 5; Aurase wound gel x9 dose concentration	Intent to treat population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	43		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	2.90 (± 1.52)	3.05 (± 1.70)		
Day 29	2.20 (± 1.62)	2.12 (± 1.99)		

Statistical analyses

No statistical analyses for this end point

Primary: Change in Study Wound Itch Burden From Baseline Measured by Numerical Rating Scale (NRS) at Day 29 (End of Study)

End point title	Change in Study Wound Itch Burden From Baseline Measured by Numerical Rating Scale (NRS) at Day 29 (End of Study)[2]

End point description:

Subject will be asked to describe the level of wound itch on a scale of 0-10: 0 being no itch, 10 being worst imaginable itch. Baseline is defined as the last non-missing value (including scheduled and unscheduled assessments) prior to the participant receiving the first study treatment

End point type	Primary

End point timeframe:

Pre-dose at day 1 (baseline) through to day 29 (end of study)

Notes:

[2] - 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: Descriptive statistics only were used in the first-in-human clinical study

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	1.20 (± 0.84)	2.11 (± 1.05)	1.60 (± 2.40)	2.00 (± 2.40)
Day 29	1.00 (± 1.23)	1.67 (± 1.50)	1.30 (± 1.25)	1.50 (± 2.45)

End point values	Cohort 5; Aurase wound gel x9 dose concentration	Intent to treat population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	2.00 (± 2.21)	1.84 (± 1.70)		
Day 29	1.30 (± 1.34)	1.38 (± 1.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Surface Area of Wound Compared to Baseline

End point title	Change in Surface Area of Wound Compared to Baseline

End point description:

Determination of surface area made by clinical assessor upon assessment of wound at each study visit.

End point type	Secondary

End point timeframe:

Day 1 (baseline), day 5, day 12, day 19, day 29 (end of study)

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: cm2				
arithmetic mean (standard deviation)				
Baseline	27.9 (± 20.1)	12.1 (± 11.2)	10.4 (± 8.2)	8.7 (± 7.1)
Day 5	25.4 (± 18.9)	12.7 (± 11.8)	9.9 (± 9.2)	8.1 (± 9.1)
Day 12	21.8 (± 18.7)	11.9 (± 11.8)	10.0 (± 9.8)	7.6 (± 9.4)
Day 19	20.9 (± 18.5)	9.4 (± 11.3)	10.6 (± 11.3)	6.9 (± 8.0)

Day29	21.8 (± 24.4)	8.8 (± 10.8)	10.1 (± 11.9)	6.2 (± 7.3)

End point values	Cohort 5; Aurase wound gel x9 dose concentration			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: cm2				
arithmetic mean (standard deviation)				
Baseline	16.8 (± 13.7)			
Day 5	14.2 (± 11.7)			
Day 12	13.0 (± 11.2)			
Day 19	13.3 (± 9.1)			
Day29	10.5 (± 8.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Achieving Different Levels of Debridement at 4 Weeks

End point title	Number of Patients Achieving Different Levels of Debridement at 4 Weeks

End point description:

Determination of debridement made by clinical assessor upon assessment of wound at each study visit. The extent of debridement is the inverse of the percentage of non-viable tissue present in the wound, where 0% debridement equates to the same percentage of non-viable tissue at baseline and 100% debridement equates to 100% removal of the non-viable tissue

End point type	Secondary

End point timeframe:

4 weeks

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: patients				
100% Debridement	0	0	1	2
>90% Debridement	2	0	2	3
>80% Debridement	3	1	5	3
>70% Debridement	3	2	6	5

End point values	Cohort 5; Aurase wound gel x9 dose concentration			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: patients				
100% Debridement	2			
>90% Debridement	3			
>80% Debridement	3			
>70% Debridement	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Surface Area of Devitalised Tissue (Slough) Compared to Baseline

End point title	Change in Surface Area of Devitalised Tissue (Slough) Compared to Baseline

End point description:

Determination of devitalised tissue made by clinical assessor upon assessment of wound at each study visit.

End point type	Secondary

End point timeframe:

Day 1 (baseline), day 5, day 12, day 19, day 29 (end of study)

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: cm2				
arithmetic mean (standard deviation)				
Baseline	7.2 (± 6.0)	7.4 (± 6.4)	7.2 (± 6.0)	6.2 (± 6.7)
Day 5	4.1 (± 4.1)	7.2 (± 7.2)	5.4 (± 4.5)	5.8 (± 8.5)
Day 12	4.6 (± 5.5)	7.9 (± 8.0)	5.3 (± 6.8)	5.0 (± 8.6)
Day 19	3.8 (± 5.1)	7.6 (± 9.7)	5.7 (± 8.8)	4.3 (± 7.0)
Day 29	2.3 (± 2.6)	5.6 (± 7.1)	4.6 (± 8.6)	4.0 (± 6.6)

End point values	Cohort 5; Aurase wound			

	gel x9 dose concentration			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: cm2				
arithmetic mean (standard deviation)				
Baseline	10.2 (± 10.2)			
Day 5	7.3 (± 8.2)			
Day 12	5.9 (± 5.3)			
Day 19	6.2 (± 5.1)			
Day 29	3.6 (± 3.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Surface Area of Granulation Tissue From Baseline

End point title	Change in Surface Area of Granulation Tissue From Baseline

End point description:

Determination of granulation tissue made by clinical assessor upon assessment of wound at each study visit.

End point type	Secondary

End point timeframe:

Day 1 (baseline) , day 5, day 12, day 19, day 29 (end of study)

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: Percent				
arithmetic mean (standard deviation)				
Baseline	75.0 (± 9.8)	33.8 (± 24.6)	33.7 (± 26.9)	25.6 (± 32.0)
Day 5	84.9 (± 10.5)	42.1 (± 24.5)	47.6 (± 28.8)	46.0 (± 35.2)
Day 12	76.4 (± 34.6)	32.8 (± 34.2)	49.0 (± 31.3)	55.2 (± 40.1)
Day 19	76.4 (± 34.6)	32.8 (± 32.2)	65.1 (± 33.9)	57.0 (± 35.7)
Day 29	77.4 (± 39.4)	39.1 (± 37.2)	74.4 (± 29.3)	62.1 (± 36.8)

End point values	Cohort 5; Aurase wound gel x9 dose concentration			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percent				

arithmetic mean (standard deviation)				
Baseline	36.2 (± 34.2)			
Day 5	59.3 (± 32.0)			
Day 12	63.1 (± 43.8)			
Day 19	61.2 (± 31.0)			
Day 29	69.6 (± 34.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic Absorption of Aurase Enzyme Assessed Through Pharmacokinetic Profiling of Blood Samples

End point title	Systemic Absorption of Aurase Enzyme Assessed Through Pharmacokinetic Profiling of Blood Samples

End point description:

The Analysis of Aurase enzyme in Human Plasma measured by Liquid chromatography-mass spectrometry (LCMS). Values of Below the limit of quantification (BLQ) (<50 ng/mL) will be substituted by zeros

End point type	Secondary

End point timeframe:

Visit 14 (end of study/early termination)

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: ng/mL				
arithmetic mean (standard deviation)				
Overall	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)

End point values	Cohort 5; Aurase wound gel x9 dose concentration			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: ng/mL				
arithmetic mean (standard deviation)				
Overall	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of the Presence of Antibodies to Aurase in Plasma (Anti-Drug Antibody [ADA] Activity) Through Applicable Laboratory Analysis of Blood Samples

End point title	Assessment of the Presence of Antibodies to Aurase in Plasma (Anti-Drug Antibody [ADA] Activity) Through Applicable Laboratory Analysis of Blood Samples

End point description:

Assay for antibodies to Aurase performed using Meso Scale Discovery electrochemiluminescence (MSD ECL). Negative results have been substituted with zeros.

End point type	Secondary

End point timeframe:

Visit 14 (end of study/early termination)

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: ng/mL				
arithmetic mean (standard deviation)				
Overall	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)

End point values	Cohort 5; Aurase wound gel x9 dose concentration			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: ng/mL				
arithmetic mean (standard deviation)				
Overall	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Systemic Clotting Factor (Fibrinogen) in Plasma From Baseline [Time Frame: Visit 2 (Baseline) and Visit 14 (end of study/early termination)]

End point title	Change in Systemic Clotting Factor (Fibrinogen) in Plasma From Baseline [Time Frame: Visit 2 (Baseline) and Visit 14 (end of study/early termination)]

End point description:

Fibrinogen plasma concentrations determined through laboratory analysis of blood samples

End point type	Secondary

End point timeframe:

Visit 2 (Baseline) and Visit 14 (end of study/early termination)

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: g/L				
arithmetic mean (standard deviation)				
Baseline	3.84 (± 0.98)	3.57 (± 0.95)	3.59 (± 1.01)	3.17 (± 1.16)
Visit 14	4.10 (± 0.74)	3.49 (± 0.71)	3.13 (± 0.94)	3.53 (± 1.40)

End point values	Cohort 5; Aurase wound gel x9 dose concentration			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: g/L				
arithmetic mean (standard deviation)				
Baseline	3.53 (± 0.97)			
Visit 14	3.34 (± 0.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Systemic Clotting Factor (Activated Partial Thromboplastin Clotting Time [APTT]) in Plasma From Baseline

End point title	Change in Systemic Clotting Factor (Activated Partial Thromboplastin Clotting Time [APTT]) in Plasma From Baseline

End point description:

APTT determined through laboratory analysis of blood samples

End point type	Secondary

End point timeframe:

Visit 2 (baseline) and Visit 14 (end of study/early termination)

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: seconds				
arithmetic mean (standard deviation)				
Baseline	26.92 (± 3.53)	27.90 (± 1.27)	28.74 (± 2.46)	28.60 (± 1.84)
Visit 14	26.93 (± 2.93)	27.86 (± 3.06)	29.04 (± 1.63)	26.99 (± 2.71)

End point values	Cohort 5; Aurase wound gel x9 dose concentration			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: seconds				
arithmetic mean (standard deviation)				
Baseline	29.51 (± 4.48)			
Visit 14	29.70 (± 4.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Systemic Clotting Factor (Prothrombin Time [PT]) From Baseline

End point title	Change in Systemic Clotting Factor (Prothrombin Time [PT]) From Baseline
End point description:	
PT determined through laboratory analysis of blood samples	
End point type	Secondary
End point timeframe:	
Visit 2 (baseline) and Visit 14 (end of study/early termination)	

End point values	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration	Cohort 4; Aurase wound gel x5 dose concentration
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	10	9
Units: seconds				
arithmetic mean (standard deviation)				
Baseline	10.78 (± 0.82)	10.69 (± 0.26)	10.86 (± 0.51)	11.70 (± 1.43)
Visit 14	10.70 (± 0.58)	10.63 (± 0.42)	11.13 (± 0.60)	11.24 (± 0.50)

End point values	Cohort 5; Aurase wound gel x9 dose concentration			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: seconds				
arithmetic mean (standard deviation)				
Baseline	11.51 (± 1.19)			
Visit 14	11.25 (± 0.77)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From time of participants informed consent to completion of study

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Cohort 1; Aurase wound gel x0 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Reporting group title	Cohort 2; Aurase wound gel x1 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Reporting group title	Cohort 3; Aurase wound gel x1.8 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Reporting group title	Cohort 4; Aurase wound gel x5 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Reporting group title	Cohort 5; Aurase wound gel x9 dose concentration

Reporting group description:

Aurase Wound Gel is reconstituted from Aurase Component A (a hydrogel) and Aurase Component B (stabilised solutions of Aurase enzyme). By diluting different strengths of Aurase Component B with Component A, specific concentrations of Aurase Wound Gels with differing Aurase contents are yielded.

Serious adverse events	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Debility			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septicaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 4; Aurase wound gel x5 dose concentration	Cohort 5; Aurase wound gel x9 dose concentration	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)	0 / 10 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Debility			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Erysipelas			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Septicaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1; Aurase wound gel x0 dose concentration	Cohort 2; Aurase wound gel x1 dose concentration	Cohort 3; Aurase wound gel x1.8 dose concentration
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	2 / 9 (22.22%)	6 / 10 (60.00%)
Injury, poisoning and procedural complications			
Inflammation of wound			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	3 / 10 (30.00%)
occurrences (all)	0	1	3
Wound complication			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Tissue irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Dysponea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	5 / 10 (50.00%)
occurrences (all)	0	0	5
Skin irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin maceration			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erysipelas			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infected skin ulcer			

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Cohort 4; Aurase wound gel x5 dose concentration	Cohort 5; Aurase wound gel x9 dose concentration	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 9 (66.67%)	5 / 10 (50.00%)	
Injury, poisoning and procedural complications			
Inflammation of wound			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Wound complication			
subjects affected / exposed	1 / 9 (11.11%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Deep vein thrombosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 9 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Iron deficiency anaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tissue irritation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Dysponea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Skin irritation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Skin maceration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Urticaria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	

Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Erysipelas			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Infected skin ulcer			
subjects affected / exposed	0 / 9 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Sepsis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Wound infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 November 2020	Protocol V1 to V2 - update of exclusion criteria, clarification on safety definitions/sections
02 June 2021	Protocol V2 to V3 - Inclusion of COVID-19 risk assessment, reduction in cohort 1 patient number, modification/clarification of endpoints, correction to discrepancies, pre-clinical information added, update to trial schedule
15 October 2021	protocol V3 to v4 - update to exploratory endpoints, addressing comments from FDA, safety review required attendees updated, off-site visit information updated
20 April 2022	Protocol V4 to V5 - modification to make study more adaptive, addition of cohorts (6&7)
20 October 2022	Protocol V5 to V6 - modification to conduct of previously added cohorts, visit window and screening period updated

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
02 January 2023	Cohorts 6 & 7 not completed, trial end declared (in line with original plan)	-

Notes:

Limitations and caveats

None reported