



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(ies).

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

| | | | |
|---|---------------------|--------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 9 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Sepsis subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Wound infection subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Metabolism and nutrition disorders Hypocalcaemia subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 10 (10.00%) 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 occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 10 (0.00%) 0 | |
| Wound complication subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 10 (10.00%) 1 | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 10 (0.00%) 0 | |
| Deep vein thrombosis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 10 (0.00%) 0 | |
| Blood and lymphatic system disorders Anaemia | | | |

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

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