

**Clinical trial results:****A Phase II/III Adaptive, Seamless, Prospective, Randomized, Controlled, Parallel, Open Multicenter Study to Assess the Safety and Efficacy of Kék Lukács Ointment Compared to Standard Silver Sulfadiazine (Dermazin®, SSD) Therapy in the Wound Healing of Patients With Partial Thickness (Second-Degree) Burns****Summary**

| | |
|--------------------------|----------------|
| EudraCT number | 2013-005124-42 |
| Trial protocol | HU |
| Global end of trial date | 29 July 2015 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 05 December 2021 |
| First version publication date | 05 December 2021 |
| Summary attachment (see zip file) | Report Synopsis (KEKLUKACS-CLIN-02_2013-005124-42_Study Report Synopsis_20151022.pdf) |

Trial information**Trial identification**

| | |
|-----------------------|-------------------|
| Sponsor protocol code | KEKLUKACS-CLIN-02 |
|-----------------------|-------------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Lukács és Társa Gyógyszerkereskedelmi Betéti TársaságLukács és Társa Gyógyszerkereskedelmi Betéti Társaság |
| Sponsor organisation address | Mártírok street 53, Iharosberény, Hungary, 8725 |
| Public contact | KÉKLUKÁCS Help Desk, AdWare Research Ltd., 36 87789073, info@adwareresearch.com |
| Scientific contact | KÉKLUKÁCS Help Desk, AdWare Research Ltd., 36 87789073, info@adwareresearch.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 | 22 October 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 July 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 July 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Primary objective

To compare the clinical efficacy of Kék Lukács ointment treatment with standard Dermazin® (SSD) therapy in wound healing; with 3D photo documentary every second day from the first day of treatment till the 22th day of treatment or till healing of the wound; by evaluating the days needed to the wound healing.

Protection of trial subjects:

In case of considerable wound pain, commonly used pain-killer medication (paracetamol, diclofenac, ibuprofen) are allowed. Necessity of analgesics and their exact dosage is recorded in the Nurse Booklet. Other routine medical treatments for concomitant diseases are allowed and accurately recorded. Other burned wounds of patients will be treated according to the Investigator's decision.

Background therapy:

In case of considerable wound pain, commonly used pain-killer medication (paracetamol, diclofenac, ibuprofen) are allowed. Necessity of analgesics and their exact dosage is recorded in the Nurse Booklet. Other routine medical treatments for concomitant diseases are allowed and accurately recorded. Other burned wounds of patients will be treated according to the Investigator's decision.

Evidence for comparator:

Control group in the study was randomized to SSD, Dermazin® cream treatment group.
Dosage and administration: The cream should be applied to a thickness between 2-4 mm onto the sterile gauze before covering the burned surface once daily until wound healing.

| | |
|---|---------------|
| Actual start date of recruitment | 03 March 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Hungary: 73 |
| Worldwide total number of subjects | 73 |
| EEA total number of subjects | 73 |

Notes:

Subjects enrolled per age group

| | |
|----------|---|
| In utero | 0 |
|----------|---|

| | |
|---|----|
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 63 |
| From 65 to 84 years | 9 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

On Day 1 at first visit, patients will undergo screening for inclusion/exclusion criteria after having provided a written Informed Consent.

Period 1

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

Arms

| | |
|------------------------------|-------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Locally applied Kék Lukács ointment |

Arm description:

The ointment should be applied to a thickness between 1-2 mm (maximum 40 g/400 cm²) onto the gauze before covering the selected burned surface once daily until wound healing.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Kék Lukács Ointment |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | External use |

Dosage and administration details:

The ointment should be applied to a thickness between 1-2 mm onto the sterile gauze before covering the burned surface once daily until wound healing.

| | |
|------------------|----------------------|
| Arm title | SSD, Dermazin® cream |
|------------------|----------------------|

Arm description:

The cream should be applied to a thickness between 2-4 mm (maximum 20-40 g/400 cm²) onto the gauze before covering the selected burned surface once daily until wound healing.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Dermazin® |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | External use |

Dosage and administration details:

The cream should be applied to a thickness between 2-4 mm onto the sterile gauze before covering the burned surface once daily until wound healing.

| Number of subjects in period 1 | Locally applied Kék Lukács ointment | SSD, Dermazin® cream |
|---------------------------------------|-------------------------------------|----------------------|
| Started | 36 | 37 |
| Completed | 36 | 37 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Locally applied Kék Lukács ointment |
|-----------------------|-------------------------------------|

Reporting group description:

The ointment should be applied to a thickness between 1-2 mm (maximum 40 g/400 cm²) onto the gauze before covering the selected burned surface once daily until wound healing.

| | |
|-----------------------|----------------------|
| Reporting group title | SSD, Dermazin® cream |
|-----------------------|----------------------|

Reporting group description:

The cream should be applied to a thickness between 2-4 mm (maximum 20-40 g/400 cm²) onto the gauze before covering the selected burned surface once daily until wound healing.

| Reporting group values | Locally applied Kék Lukács ointment | SSD, Dermazin® cream | Total |
|------------------------|-------------------------------------|----------------------|-------|
| Number of subjects | 36 | 37 | 73 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|----------------------|----------|----------|----|
| Age continuous | | | |
| Units: years | | | |
| median | 46.7 | 52 | |
| full range (min-max) | 19 to 80 | 20 to 85 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 19 | 17 | 36 |
| Male | 17 | 20 | 37 |

Subject analysis sets

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Intent-to-treat (ITT) analysis set |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

All randomised subjects who received at least one study treatment and had at least one postbaseline evaluation of the target wound area.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Per protocol (PP) analysis set |
| Subject analysis set type | Per protocol |

Subject analysis set description:

All randomised subjects who received at least one study treatment and had at least one postbaseline evaluation of the target wound area and did not have any major protocol deviations

(protocol violation). Protocol violation included:

violation of any inclusion/exclusion criterion

randomisation error

use of any prohibited systemic or topical medication on the test site and/or on other

(non-target) burn area(s)

missing more than one clinical visits (treatment and/or follow-up).

Patients who experienced deterioration of the target wound due to treatment failure and needed therefore skin transplantation on the target wound were withdrawn from the study. If the surgery area exceeded 50% of the original wound area the patient was excluded from the PP analysis. If the surgery area did not exceed 50% of the original wound area the patient remained in the PP analysis set and the healing of the wound area outside the surgical area was taken into account for the analysis.

| | |
|----------------------------|---------------------|
| Subject analysis set title | Safety analysis set |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All randomised subjects who received at least one study treatment.

| Reporting group values | Intent-to-treat (ITT) analysis set | Per protocol (PP) analysis set | Safety analysis set |
|--|---------------------------------------|-----------------------------------|---------------------|
| Number of subjects | 73 | 70 | 73 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years median full range (min-max) | 50 19 to 85 | 32 19 to 85 | 50 19 to 85 |
| Gender categorical Units: Subjects | | | |
| Female Male | | | |

End points

End points reporting groups

| | |
|---|-------------------------------------|
| Reporting group title | Locally applied Kék Lukács ointment |
| Reporting group description: The ointment should be applied to a thickness between 1-2 mm (maximum 40 g/400 cm ²) onto the gauze before covering the selected burned surface once daily until wound healing. | |
| Reporting group title | SSD, Dermazin® cream |
| Reporting group description: The cream should be applied to a thickness between 2-4 mm (maximum 20-40 g/400 cm ²) onto the gauze before covering the selected burned surface once daily until wound healing. | |
| Subject analysis set title | Intent-to-treat (ITT) analysis set |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All randomised subjects who received at least one study treatment and had at least one postbaseline evaluation of the target wound area. | |
| Subject analysis set title | Per protocol (PP) analysis set |
| Subject analysis set type | Per protocol |
| Subject analysis set description: All randomised subjects who received at least one study treatment and had at least one postbaseline evaluation of the target wound area and did not have any major protocol deviations (protocol violation). Protocol violation included: violation of any inclusion/exclusion criterion randomisation error use of any prohibited systemic or topical medication on the test site and/or on other (non-target) burn area(s) missing more than one clinical visits (treatment and/or follow-up). Patients who experienced deterioration of the target wound due to treatment failure and needed therefore skin transplantation on the target wound were withdrawn from the study. If the surgery area exceeded 50% of the original wound area the patient was excluded from the PP analysis. If the surgery area did not exceed 50% of the original wound area the patient remained in the PP analysis set and the healing of the wound area outside the surgical area was taken into account for the analysis. | |
| Subject analysis set title | Safety analysis set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All randomised subjects who received at least one study treatment. | |

Primary: Wound healing

| | |
|---|---------------|
| End point title | Wound healing |
| End point description: The primary endpoint of this study will be the number of days until wound healing. Wound healing will be attained on the first day when the wound area (as measured by planimetry, taking the mean of the values evaluated by two independent assessors) will be below 10% of the baseline wound area. Wound area will be measured in each two days starting from baseline, and no interpolation for wound area will be performed. A wound is considered to be healed on the first day when the unhealed wound extent decreases under 10% of the original wound extent. For patients by whom treatment was continued by surgery the day of ordering surgery will be taken into consideration. If the surgery area extends 50% of the original wound area the patient will be excluded from the analysis of PP population. By the analysis the healing of the wound area outside the surgical area will be taken into account. | |
| End point type | Primary |
| End point timeframe: from baseline until wound healing | |

| End point values | Locally applied Kék Lukács ointment | SSD, Dermazin® cream | Intent-to-treat (ITT) analysis set | Per protocol (PP) analysis set |
|-----------------------------|-------------------------------------|----------------------|------------------------------------|--------------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 36 | 37 | 73 | 70 |
| Units: percentage | 36 | 37 | 73 | 70 |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Primary Efficacy Endpoint |
| Comparison groups | Locally applied Kék Lukács ointment v SSD, Dermazin® cream |
| Number of subjects included in analysis | 73 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 |
| Method | t-test, 1-sided |

| | |
|---|--|
| Statistical analysis title | Primary Efficacy Endpoint |
| Comparison groups | Locally applied Kék Lukács ointment v SSD, Dermazin® cream |
| Number of subjects included in analysis | 73 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Signs of wound infection and Inflammation

| | |
|------------------------|---|
| End point title | Signs of wound infection and Inflammation |
| End point description: | Investigator's assessment of signs of wound infection and inflammation: a) oozing, b) erythema, c) warmth, d) oedema, e) pain, f) odour on each medical visit in treatment and follow up periods of the study |
| End point type | Secondary |
| End point timeframe: | From Visit 1 to Follow-up Visit 2 |

| End point values | Locally applied Kék Lukács ointment | SSD, Dermazin® cream | Intent-to-treat (ITT) analysis set | |
|-----------------------------|-------------------------------------|----------------------|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 36 | 37 | 73 | |
| Units: percentage | 36 | 37 | 73 | |

Statistical analyses

| Statistical analysis title | Signs of wound infection and Inflammation |
|---|--|
| Statistical analysis description: | |
| The following secondary efficacy parameters were evaluated: | |
| <ul style="list-style-type: none"> - signs of wound infection - inflammation - pain scores - cosmetic results | |
| The proportions of number of subjects healed until a certain day were calculated and compared between treatment arms, with 95% confidence intervals. | |
| <ul style="list-style-type: none"> - percent reduction of wound area - wound margin - wound bed - wound surface - wound secretion - proportion of subjects receiving skin transplantation | |
| Comparison groups | SSD, Dermazin® cream v Locally applied Kék Lukács ointment |
| Number of subjects included in analysis | 73 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Median difference (final values) |

Secondary: Wound-related mean pain scores

| End point title | Wound-related mean pain scores |
|------------------------------------|--------------------------------|
| End point description: | |
| Wound related pain after treatment | |
| End point type | Secondary |
| End point timeframe: | |
| From study day 1 to day 29 | |

| End point values | Locally applied Kék Lukács ointment | SSD, Dermazin® cream | | |
|--|-------------------------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 36 | 37 | | |
| Units: pain | | | | |
| geometric mean (confidence interval 95%) | 1 (1 to 2.7) | 2.7 (1 to 2.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cosmetic Results

| | |
|-----------------|------------------|
| End point title | Cosmetic Results |
|-----------------|------------------|

End point description:

Comprising only subjects with not censored data

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Visit 3 to Follow-up visit 2

| End point values | Locally applied Kék Lukács ointment | SSD, Dermazin® cream | | |
|-----------------------------|---|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 36 | 37 | | |
| Units: percentage | 36 | 37 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | General Cosmetic Results |
| Comparison groups | SSD, Dermazin® cream v Locally applied Kék Lukács ointment |
| Number of subjects included in analysis | 73 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | Wilcoxon (Mann-Whitney) |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From 19.06.2014 to 29.04.2015

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Severity |
|-----------------------|----------|

Reporting group description: -

| Serious adverse events | Severity | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Skin graft | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Condition aggravated | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Severity | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 73 (39.73%) | | |
| Injury, poisoning and procedural complications | | | |
| Wound complication | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Arthropod sting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>15 / 73 (20.55%)</p> <p>15</p> <p>1 / 73 (1.37%)</p> <p>1</p> | | |
| <p>Cardiac disorders</p> <p>Hypertension</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 73 (1.37%)</p> <p>1</p> | | |
| <p>Nervous system disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dizziness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 73 (1.37%)</p> <p>1</p> <p>1 / 73 (1.37%)</p> <p>1</p> | | |
| <p>General disorders and administration site conditions</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Chills</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 73 (5.48%)</p> <p>5</p> <p>1 / 73 (1.37%)</p> <p>1</p> | | |
| <p>Immune system disorders</p> <p>Rhinitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 73 (1.37%)</p> <p>1</p> | | |
| <p>Gastrointestinal disorders</p> <p>Dry mouth</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> | <p>1 / 73 (1.37%)</p> <p>1</p> <p>1 / 73 (1.37%)</p> <p>1</p> | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | | |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 3 | | |
| Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 1 / 73 (1.37%) 1 | | |
| Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | | |
| Infections and infestations Cystitis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 1 / 73 (1.37%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 28 February 2014 | The reason of the modification is the notes of ETT and GYEMSZI-OGYI to the first version of the protocol (December 16, 2013) |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported