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 analy	
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 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.

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 analy

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:
- 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.
- 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			

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

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