A Phase IIb, prospective, intra-patient randomised controlled, multicentre study to evaluate the safety and efficacy of an autologous bio-engineered dermo-epidermal skin substitute (EHSG-KF) for the treatment of partial deep dermal and full thickness burns in children in comparison to autologous split-thickness skin grafts (STSG)

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To evaluate the efficacy and safety of EHSG-KF in comparison to meshed STSG in children with partial deep dermal and full thickness burns. Primary Objective: To evaluate the efficacy of EHSG-KF in comparison to meshed STSG based on:• Ratio of...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55737

Source
ToetsingOnline

Brief title
TBRU-dS-BC-PIIb

Condition

- Other condition

Synonym
dermal burns, skin damage due to heat

Health condition

ernstige brandwonden

Research involving
Human

Sponsors and support

Primary sponsor: CUTISS AG
Source(s) of monetary or material Support: Wyss Zurich

Intervention

Keyword: Acute burns, Skin graft, Tissue engineering, Transplant

Outcome measures

Primary outcome

Primary Endpoint

Efficacy evaluation, as a comparison between the EHSG-KF and control sites,

based on:

• Ratio of covered surface area to biopsy site/donor site surface area at visit

6(28 +/-3 days post grafting)

Secondary outcome

First secondary efficacy endpoint:

• % Epithelialization at:

o visit 8 (90 ± 5 days post grafting)

Secondary Endpoints

Safety and efficacy evaluation, as a comparison between the EHSG-KF and control sites, based on:

• Main secondary safety endpoint:

Clinical and microbiologic signs of infection at visits 4 (6-10 days post grafting) and 5 (21 +/-2 days post grafting)

• Main secondary efficacy endpoints:

Scar quality at the study areas

Assessment of elasticity of the study areas using the Cutometer® at visit 10 (1 year +/-30 days post grafting)

o Assessment of general scar quality at the study areas using the POSAS, a reliable and validated scar assessment tool, at visit 10 (1 year +/-30 days post grafting)

• Other secondary safety endpoint:

Assessment and reporting of all observed adverse events will be carried out for the full duration of the study from visit 2 on

• Other secondary efficacy endpoint:

Epithelialization at visit 6 (28 +/-3 days post grafting)

Study description

Background summary

The management of severe burns remains a significant challenge. The current gold standard, excision and coverage with meshed STSG, is limited by both donor site availability and the risk of disfiguring and functionally debilitating scars. The introduction of cultured epithelial autografts (CEA) has helped

address donor site limitations; however, thirty years since its introduction, despite tremendous research efforts, CEA continues to yield unacceptable results when used independently for the coverage of deep burns. The role of CEA in contemporary burn care is, therefore, largely adjunctive, as is the case with other keratinocyte replacement techniques, such as keratinocyte spray. The clinical introduction of now widely used dermal regeneration templates (e.g. IntegraDRT® and Matriderm®) has pushed the frontiers further, with potential for improved aesthetic and functional results. However, such templates still require coverage with an overlying skin graft. The evolution of an autologous tissue-engineered skin substitute, such as EHSG-KF, that can be used as an alternative to a STSG, represents the next step towards achieving coverage of severe burns with limited donor sites, thereby offering a potentially lifesaving therapy.

EHSG-KF is a tissue-engineered autologous dermo-epidermal skin substitute for the treatment of partial deep dermal and full thickness skin burns.
The proposed phase IIb clinical trial aims to evaluate the safety and efficacy of EHSG-KF in adult patients with severe burns, when compared to meshed STSG, the current gold standard.

Study objective

To evaluate the efficacy and safety of EHSG-KF in comparison to meshed STSG in children with partial deep dermal and full thickness burns.
Primary Objective: To evaluate the efficacy of
EHSG-KF in comparison to meshed STSG based on:
• Ratio of covered surface area to biopsy site/donor site surface area 4 weeks post grafting

First Secondary Objective
• % Epithelialization at 3 months post grafting

Secondary Objectives:
To evaluate the safety and efficacy of EHSG-KF in comparison to meshed STSG based on the assessment of:
• Infection
• Scar quality:
o Cutometer® 3, 6, 12, 24 and 36 months post grafting
o DSM ColorMeter® 3, 6, 12, 24 and 36 months post grafting
o POSAS-questionnaire 3, 6, 12, 24 and 36 months post grafting

• Graft take at 6-10 days post grafting
• %Epithelialization (to estimate *time to complete epithelialization*) at 3 and 4 weeks, and 2 and 6 months post grafting
• Incidence of wound closure at 8 and 12 weeks post grafting
• Assessment and reporting of all observed adverse events
• QOL assessment (EQ-5D and BSHS-B)

• Healthcare resource utilization (direct and indirect healthcare costs, this questionnaire will not be handed out to patients)

Study design

Open label, intra-patient randomised controlled, prospective, multicentre phase IIb clinical trial
Intra-patient randomization: Two sites, A and B, each an area of 45-90 cm2 are selected. Each site is covered either with a meshed STSG, or EHSG-KF, and the type of graft for each site has been determined in advance.
The endpoint measures described above, including ratio of covered surface area to harvested surface area and presence of infection, will be determined for each site, and comparisons made

Intervention

Product:
EHSG-KF is an autologous tissue-engineered dermo-epidermal skin substitute on a collagen type I hydrogel. The size per graft is 45±4cm2 and the thickness is 0.5-2 mm.

Intervention:
Grafting of the wound bed (=experimental area) with 1 to 2 grafts of EHSG-KF

Product (control):
Autologous split-thickness skin graft (STSG) meshed at a ratio of 3:1
Intervention:
Grafting of the control wound bed (=control area) with meshed STSG, whereby size of control area=size of experimental area

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness (if applicable): Klik voor meer informatie

The experimental product potentially offers a better therapeutic option than STSG alone. EHSG-KF has been successfully tested in the phase I clinical trial and several preclinical studies without significant adverse reactions and, as the skin grafts are autologous, no unusually high incidence of complications/adverse effects is anticipated. If the working hypothesis proves true, then graft take and wound healing dynamics will be similar to those of STSG, while the efficacy, in terms of scar quality and final functional and cosmetic results, will be even better than obtained from STSG alone. Currently the product is under investigation and ongoing risk will be assessed and risk

mitigation strategies are included in the study protocol. Based on the available study results, we do not believe the risk associated with this product is greater than the usual treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

• Age: <12 years of age
• Deep partial thickness and/or full-thickness burns requiring surgical wound coverage
• Expected that >=90 cm2 of wound (not counting the head and neck area for study patients in The Netherlands) will remain open at 4 weeks post burn despite proceeding with treatment in accordance with the standard

of care. >20% TBSA burns can be taken as guideline, but TBSA is not an inclusion criterion.
• Signed informed consent from the patient or the parents/legally authorized representative.

Exclusion criteria

Patients tested positive for HBV, HCV, syphilis or HIV
• Patients with known underlying or concomitant medical conditions that may interfere with normal wound healing (e.g. systemic skin and connective tissue diseases, any kind of congenital defect of metabolism including insulin-dependent diabetes mellitus, Cushing syndrome or disease, scurvy, chronic hypothyroidism, congenital or acquired immunosuppressive condition, chronic renal failure, or chronic hepatic dysfunction (Child-Pugh class B or C), severe malnutrition, or other concomitant illness which, in the opinion of the Investigator, has the potential to significantly delay wound healing)
• Severe drug and alcohol abuse
• Pre-existing coagulation disorders as defined by INR outside its normal value, PTT >ULN and fibrinogen / or at the Investigator*s discretion
• Patients with known allergies to amphotericin B, gentamicin, penicillin or streptomycin or bovine collagen
• Previous enrolment of the patient into the current phase II study
• Participation of the patient in another study with conflicting endpoints within 30 days preceding and during the present study
• Patients or parents/legal guardian expected not to comply with the study protocol (including patients with severe cognitive dysfunction/impairment and severe psychiatric disorders)
• Pregnant or breast feeding females
• Suspicion of non-accidental injury
•Wounds in the head and neck area as study target area (only applicable for study patients in The Netherlands)
• Enrolment of the Investigator, his/her family members, employees and other dependent persons

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2017
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	12-09-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-10-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-07-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-08-2019
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-09-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-11-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-12-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-05-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-06-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-10-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-11-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	07-04-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-05-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-05-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-12-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-02-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-03-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-04-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	17-05-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-07-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-07-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-08-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-002461-21-NL

Register	ID
CCMO	NL62416.000.17