A Phase II, 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 full thickness skin defects in adults and children in comparison to autologous split-thickness skin grafts (STSG)

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This study has been transitioned to CTIS with ID 2024-512190-27-00 check the CTIS register for the current data. To evaluate the efficacy and safety of EHSG-KF in comparison to STSG (unmeshed or meshed up to 1:3) in adults and children with large...

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

Summary

ID

NL-OMON56452

Source
ToetsingOnline

Brief title
TBRU-dS-RAC-PII

Condition

- Other condition

Synonym
Skin abnormality, skin condition

Health condition

Grote huiddefecten

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Skin defects, 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 assessment of general scar quality at the study areas using the POSAS

questionnaire, observer total score at: visit 8 (90 days +/-5 days post

grafting)

Secondary outcome

Secondary Endpoints

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

based on:

- Scar quality at the study areas in comparison to control areas:

o Cutometer® pliability parameter at visit 8 (90 days +/-5 days post grafting) as key secondary efficacy endpoint

o Other Cutometer® parameters (extension, elasticity, retraction, viscoelasticity) at visit 8 (90 days +/-5 days post grafting)

o POSAS questionnaire observer items (vascularity, pigmentation, thickness, relief, pliability) at visit 8 (90 days +/-5 days post grafting)

o POSAS questionnaire patient items (pain, itching, color, pliability, thickness, relief) and total score at visit 8 (90 days +/-5 days after grafting)

o DSM ColorMeter® (erythema and pigmentation) at: visit 10 (1 year +/-30 days post grafting)

o Biopsies of the study area and control area at visit 10 (1 year +/-30 days after grafting) for histological assessment. (optional)

o Graft take at Visit 4 (6-10 days after grafting)

o % Epithelialization at Visit 6 (28 days +/- 3 days after grafting)

Secondary safety endpoints:

- Clinical and microbiologic signs of infection at

o visits 4 (6-10 days post grafting)

o visit 5 (21 +/-2 days post grafting)

- Adverse events

o 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:

- QOL assessment: visit 10 (1 year +/-30 days post grafting)

o EQ-5D and BSHS-B for patients >=18 years with reconstruction of a burn scar

o EQ-5D only for patients >=18 years without burn scars

o EQ-5DY and PedsQLpatients <18 years

Study description

Background summary

Large full thickness skin defects requiring definitive coverage are frequently encountered in various contexts in both children and adults. They typically result from injuries (e.g. burns, injuries), illness (e.g. septic skin necrosis), or when extended (re)constructive surgical procedures are to be performed. The coverage of such extended lesions still poses a very significant challenge: the functionally and cosmetically best therapeutic option would be transplanting full thickness autologous skin, as this basically leads to reconstitution of a normal skin in terms of both function and cosmetics. However, donor sites are limited in a prohibitive way when there is extensive demand (>2-3% total body surface area (TBSA)). By using a dermal template (e.g. Integra Regenerative Template) in combination with a STSG the functional and aesthetic outcome can be improved, but will never reach the outcome of full thickness skin grafts. Furthermore, the two stage procedure is highly time consuming (e.g. 5/6 weeks in reconstructive procedures), since the formation of a neodermis has to be awaited before the STSG can be done.
In view of all above considerations, in particular based on the fact that only full thickness skin transplants yield truly excellent long-term results when the entire skin has to be replaced, the vision to build autologous skin analogues in the laboratory by means of tissue engineering has been developed.

The proposed phase II clinical trial aims to evaluate the safety and efficacy of EHSG-KF, a bioengineered autologous dermo-epidermal skin substitute, in adults and children with large skale full thickness skin defects, when compared to split-thickness skin grafts (STSG), the current gold standard.

Study objective

This study has been transitioned to CTIS with ID 2024-512190-27-00 check the CTIS register for the current data.

To evaluate the efficacy and safety of EHSG-KF in comparison to STSG (unmeshed or meshed up to 1:3) in adults and children with large full thickness skin

defects.

Primary Objective:
To evaluate the efficacy of EHSG-KF in comparison to STSG based on the assessment of:
- Scar quality:
o POSAS questionnaire, observer total score 3 months post grafting

Secondary Objectives
To evaluate the safety and efficacy of EHSG-KF in comparison to STSG (unmeshed or meshed up to 1:3) based on the assessment of:
- Scar quality:
o Cutometer® 3 months post grafting
o POSAS questionnaire, observer items 3 months post grafting
o POSAS questionnaire, patient items and total score 3 months post grafting
o DSM ColorMeter® (1 year post grafting)
o Biopsies of the study area and control area (1 year post grafting) for histological assessment. (optional)
- Infection 6-10 days and 3 weeks post grafting
- Graft take at 6-10 days post grafting
- % Epithelialization at 4 weeks post grafting
- Adverse events
- QOL assessment at (1 year) post grafting
o EQ-5D and BSHS-B for patients >=18 years with reconstruction of burn scars,
o EQ-5D only for patients >=18 years without burn scars,
o EQ-5DY and PedsQL for patients <18 years
- Ratio of covered surface area to biopsy site/donor site surface area 4 weeks post grafting

Study design

Open label, intra-patient randomised, prospective, multi-centre phase II clinical trial.
Intra-patient randomisation means that each patient has 2 spots, A and B, each with a size of 45-90cm2 that are selected. Each spot is covered with either the standard method (meshed STSG) or EHSG-KF, and it is determined in advance which treatment will be applied to which spot. The endpoints are measured and compared.

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.

Study burden and risks

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
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

• Age: >=1 year of age

•Large full-thickness defects that require coverage after excision of:
-Scars
-Benign skin tumors (e.g. neurofibroma)
-Melanocytic nevus (e.g. giant nevus)
- Gender reassignment surgery
-Soft tissue defect after trauma
-Soft tissue defect after infection and debridement (e.g. necrotizing fascitis, hidradentitis suppurativa, purpura fulminans)
-Flap donor site (e.g. radial forearm flap)

•Minimal areas requiring coverage (not counting the head and neck area for study patients in The Netherlands):
-Minimum: 1-5 years: 9 cm2
- Minimum: 6-16 years: 25 cm2
-Minimum: > 16 years: 45 cm2

•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

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-05-2019
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	01-02-2018
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:	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:	18-05-2020
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:	11-10-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-11-2023
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
EU-CTR	CTIS2024-512190-27-00
EudraCT	EUCTR2017-002462-41-NL
CCMO	NL64565.000.18