Clinical trial results:
Evaluation of the safety and efficacy of the treatment of scars and cutis laxa syndrome with the use of autologous (fresh and stored) stem cells isolated from adipose tissue within the project: 'The therapeutic potential of mesenchymal stem cells tested in clinical trials and in vitro - a justification for characterized cells storage'.

Summary

EudraCT number	2016-004110-10
Trial protocol	PL
Global end of trial date	18 January 2020

Results information

Result version number	v1 (current)
This version publication date	24 June 2021
First version publication date	24 June 2021
Summary attachment (see zip file)	SUMMARY_2ABC_clinical_trial (streszczenie_EMA (002).pdf)

Trial information

Trial identification

Sponsor protocol code	2ABC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03887208
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University of Warsaw
Sponsor organisation address	ul. Żwirki i Wigury 61, Warszawa, Poland, 02-091
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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	18 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the study was to demonstrate the safety and efficacy of autologous adipose tissue-derived stem cells - fresh (SVF fraction) or cryopreserved (ADSC fraction), delivered via topical injection in patients with scarring or cutis laxa of the dorsal surface of the hands.

Protection of trial subjects:

The study protocol and all changes to this document and patient information card have been reviewed and approved by the appropriate independent ethics committees. The study was conducted in accordance with the current version of the declaration of Helsinki. The study was conducted in accordance with the Good Clinical Practice (GCP) guidelines of the International Conference on Harmonization (ICH). Before the study, all patients gave written informed consent to participate in the study. The study procedures (objectives, methodology, potential risks, anticipated benefits) were detailed in the patient information card and explained to each patient by the investigator.

In order to protect patients, the following medications were used:
Midazolam - premedication, relieving tension before surgery
EMLA (Lidocaine + Prilocaine) - analgesic
Tumescent fluid - infiltration anesthesia
Augmentin - infection prevention
Low molecular weight heparin - antithrombotic prevention

Background therapy:

Before the mesotherapy treatment/placebo administration, all patients underwent a non-ablative fractional laser treatment aimed at stimulating collagen renewal, which is used in the treatment of scars and keloids, smoothing the skin surface and improving skin tone. The laser setting parameters in all patients were the same, in low standard ranges recommended for a given area and type of changes/indications in the patient.

Before liposuction, anticoagulant treatment with low molecular weight heparin in a standard dose, oral antibiotic (Augmentin 1.0 g) or intravenous (Tarcefandol 1.0 g - second generation cephalosporin) and premedication (Midazolam 7.5-15 mg) were used. Operation fields were prepared as for a surgical procedure, i.e. washed with a disinfectant.

Before the laser therapy and mesotherapy, Emla cream with lignocaine and 5% prilocaine or prescription cream with 23% lignocaine was used (40-60 min). They were washed off before the procedure.

Allowed emergency treatment included:
- causal treatment of emergency medical conditions directly life-threatening,
- systemic antibiotic therapy in the case of bacterial infections up to 10 days,
- topical treatment with antiseptics (octenisept, boric acid, chlorhexidine).

Evidence for comparator:

Studied therapy was compared to placebo.

Actual start date of recruitment	31 January 2018
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	Poland: 112
Worldwide total number of subjects	112
EEA total number of subjects	112

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)	99
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patient recruitment to the clinical trial started on 31.01.2018. The first patient was enrolled to the study on 31.01.2018 and the last patient on 23.05.2019. Patients were recruited in two research centers: Timeless Chirurgia Plastyczna spółka z o.o., Warsaw, Poland and Melitus Sp. z o o, Warsaw, Poland.

Pre-assignment

Screening details:

The number of patients planned for inclusion was 100. 127 patients were recruited (signed consent to participate in the study) in two clinical sites: 72 at Site 1 and 55 at Site 2. 15 patients did not pass the screening. 112 patients were randomized - 92 to arm A (active treatment) and 20 to arm B (placebo).

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

In arm A patients with cutis laxa or scarring received a dose of stem cell suspension isolated from lipoaspirate and then injected into the patient's skin. Patients received treatment in two schemes. In Scheme I (SVF) patients received a fresh fraction of cells isolated from adipose tissue (not subjected to in vitro culture). This is the so-called stromal vascular fraction. Some SVF cells were frozen and some were prepared in cell culture for the second and subsequent applications in the patient. In Scheme II (ADSC) the first application of the cultured cell suspension took place 6-12 days after the liposuction/lipoaspiration procedure. Some cells were cryopreserved and after thawing prepared in cell culture for the second and subsequent applications in the patient.

Arm type	Experimental
Investigational medicinal product name	Adipose tissue-derived mesenchymal stem cells
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A dose of stem cell suspension isolated from lipoaspirate and then injected into the patient's skin

Arm title	Placebo

Arm description:

In arm B, placebo was administered to a hand or two scars or a single scar. The placebo was a 0.9% NaCl (saline) solution injected using the same procedure as for the stem cell suspension.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The placebo was a 0.9% NaCl (saline) solution injected using the same procedure as for the stem cell suspension.

Number of subjects in period 1	Arm A	Placebo
Started	92	20
Completed	74	20
Not completed	18	0
Consent withdrawn by subject	12	-
preparation of product was imposible	4	-
Adverse event, non-fatal	2	-

Baseline characteristics

Reporting groups	
Reporting group title	overall trial (overall period)
Reporting group description: -	

Reporting group values	overall trial (overall period)	Total	
Number of subjects	112	112	
Age categorical			
Subjects aged 18-75 years were enrolled in the trial			
Units: Subjects			
Adults (18-75 years)	112	112	
Gender categorical Units: Subjects			
Female	103	103	
Male	9	9	

Subject analysis sets	
Subject analysis set title	All patients
Subject analysis set type	Full analysis
Subject analysis set description: Full analysis	
Subject analysis set title	Arm A Scarring SVF
Subject analysis set type	Full analysis
Subject analysis set description: Patients with scarring, administered active treatment in Scheme I (SVF)	
Subject analysis set title	Arm A Cutis laxa SVF
Subject analysis set type	Full analysis
Subject analysis set description: Patients with cutis laxa, administered active treatment in Scheme I (SVF)	
Subject analysis set title	Arm A Cutis laxa ADSC
Subject analysis set type	Full analysis
Subject analysis set description: Patients with cutis laxa, administered active treatment in Scheme II (ADSC)	
Subject analysis set title	Arm A Scarring ADSC
Subject analysis set type	Full analysis
Subject analysis set description: Patients with scarring, administered active treatment in Scheme II (ADSC)	
Subject analysis set title	Arm B Cutis laxa ADSC
Subject analysis set type	Full analysis
Subject analysis set description: Patients with cutis laxa, administered placebo in Scheme II (ADSC)	
Subject analysis set title	Arm B Scarring ADSC
Subject analysis set type	Full analysis
Subject analysis set description: Patients with scarring, administered placebo in Scheme II (ADSC)	
Subject analysis set title	Arm B Cutis laxa SVF

Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with cutis laxa, administered placebo in Scheme I (SVF)	
Subject analysis set title	Arm B Scarring SVF
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with scarring administered placebo in Scheme I (SVF)	
Subject analysis set title	Arm A ADSC
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients administered active treatment in Scheme II (ADSC)	
Subject analysis set title	Arm A SVF
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients administered active treatment in Scheme I (SVF)	
Subject analysis set title	Arm B ADSC
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients administered placebo in Scheme II (ADSC)	
Subject analysis set title	Arm B SVF
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients administered placebo in Scheme I (SVF)	
Subject analysis set title	Arm A Scarring
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with scarring administered active treatment	
Subject analysis set title	Arm A Cutis laxa
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with cutis laxa, administered active treatment	
Subject analysis set title	Arm B Scarring
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with scarring, administered placebo	
Subject analysis set title	Arm B Cutis laxa
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with cutis laxa, administered placebo	

Reporting group values	All patients	Arm A Scarring SVF	Arm A Cutis laxa SVF
Number of subjects	94	18	17
Age categorical			
Subjects aged 18-75 years were enrolled in the trial			
Units: Subjects			
Adults (18-75 years)	94	18	17
Gender categorical Units: Subjects			
Female	86	15	17
Male	8	3	0

Reporting group values	Arm A Cutis laxa ADSC	Arm A Scarring ADSC	Arm B Cutis laxa ADSC
Number of subjects	20	19	5
Age categorical			
Subjects aged 18-75 years were enrolled in the trial			
Units: Subjects			
Adults (18-75 years)	19	19	5
Gender categorical Units: Subjects			
Female	19	16	5
Male	1	3	0

Reporting group values	Arm B Scarring ADSC	Arm B Cutis laxa SVF	Arm B Scarring SVF
Number of subjects	5	5	5
Age categorical			
Subjects aged 18-75 years were enrolled in the trial			
Units: Subjects			
Adults (18-75 years)	5	5	5
Gender categorical Units: Subjects			
Female	5	5	4
Male	0	0	1

Reporting group values	Arm A ADSC	Arm A SVF	Arm B ADSC
Number of subjects	39	35	10
Age categorical			
Subjects aged 18-75 years were enrolled in the trial			
Units: Subjects			
Adults (18-75 years)	38	35	10
Gender categorical Units: Subjects			
Female	35	32	10
Male	4	3	0

Reporting group values	Arm B SVF	Arm A Scarring	Arm A Cutis laxa
Number of subjects	10	37	37
Age categorical			
Subjects aged 18-75 years were enrolled in the trial			
Units: Subjects			
Adults (18-75 years)	10	37	36
Gender categorical Units: Subjects			
Female	9	31	36
Male	1	6	1

Reporting group values	Arm B Scarring	Arm B Cutis laxa	
Number of subjects	10	10	
Age categorical			
Subjects aged 18-75 years were enrolled in the trial			
Units: Subjects			
Adults (18-75 years)	10	10	

Gender categorical Units: Subjects			
Female	9	10	
Male	1	0	

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
In arm A patients with cutis laxa or scarring received a dose of stem cell suspension isolated from lipoaspirate and then injected into the patient's skin. Patients received treatment in two schemes. In Scheme I (SVF) patients received a fresh fraction of cells isolated from adipose tissue (not subjected to in vitro culture). This is the so-called stromal vascular fraction. Some SVF cells were frozen and some were prepared in cell culture for the second and subsequent applications in the patient. In Scheme II (ADSC) the first application of the cultured cell suspension took place 6-12 days after the liposuction/lipoaspiration procedure. Some cells were cryopreserved and after thawing prepared in cell culture for the second and subsequent applications in the patient.	
Reporting group title	Placebo
Reporting group description:	
In arm B, placebo was administered to a hand or two scars or a single scar. The placebo was a 0.9% NaCl (saline) solution injected using the same procedure as for the stem cell suspension.	
Subject analysis set title	All patients
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis	
Subject analysis set title	Arm A Scarring SVF
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with scarring, administered active treatment in Scheme I (SVF)	
Subject analysis set title	Arm A Cutis laxa SVF
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with cutis laxa, administered active treatment in Scheme I (SVF)	
Subject analysis set title	Arm A Cutis laxa ADSC
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with cutis laxa, administered active treatment in Scheme II (ADSC)	
Subject analysis set title	Arm A Scarring ADSC
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with scarring, administered active treatment in Scheme II (ADSC)	
Subject analysis set title	Arm B Cutis laxa ADSC
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with cutis laxa, administered placebo in Scheme II (ADSC)	
Subject analysis set title	Arm B Scarring ADSC
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with scarring, administered placebo in Scheme II (ADSC)	
Subject analysis set title	Arm B Cutis laxa SVF
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with cutis laxa, administered placebo in Scheme I (SVF)	
Subject analysis set title	Arm B Scarring SVF
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients with scarring administered placebo in Scheme I (SVF)	

Subject analysis set title	Arm A ADSC
Subject analysis set type	Full analysis
Subject analysis set description: Patients administered active treatment in Scheme II (ADSC)	
Subject analysis set title	Arm A SVF
Subject analysis set type	Full analysis
Subject analysis set description: Patients administered active treatment in Scheme I (SVF)	
Subject analysis set title	Arm B ADSC
Subject analysis set type	Full analysis
Subject analysis set description: Patients administered placebo in Scheme II (ADSC)	
Subject analysis set title	Arm B SVF
Subject analysis set type	Full analysis
Subject analysis set description: Patients administered placebo in Scheme I (SVF)	
Subject analysis set title	Arm A Scarring
Subject analysis set type	Full analysis
Subject analysis set description: Patients with scarring administered active treatment	
Subject analysis set title	Arm A Cutis laxa
Subject analysis set type	Full analysis
Subject analysis set description: Patients with cutis laxa, administered active treatment	
Subject analysis set title	Arm B Scarring
Subject analysis set type	Full analysis
Subject analysis set description: Patients with scarring, administered placebo	
Subject analysis set title	Arm B Cutis laxa
Subject analysis set type	Full analysis
Subject analysis set description: Patients with cutis laxa, administered placebo	

Primary: Time taken to see a 50% improvement in the patient's quality of life score from baseline

End point title	Time taken to see a 50% improvement in the patient's quality of life score from baseline
End point description:	
End point type	Primary
End point timeframe: Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study	

End point values	Arm A	Placebo	Arm A Scarring SVF	Arm A Cutis laxa ADSC
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	74	20	18	19
Units: weeks				
arithmetic mean (standard error)	22.6 (± 0.8)	23.4 (± 1.6)	23.3 (± 1.7)	21.5 (± 2.0)

End point values	Arm A Scarring ADSC	Arm B Cutis laxa ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	5	5	5
Units: weeks				
arithmetic mean (standard error)	21.3 (± 2.1)	25.5 (± 0.0)	25.5 (± 0.0)	17.1 (± 4.6)

End point values	Arm A ADSC	Arm A SVF	Arm B ADSC	Arm B SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38	35	10	10
Units: weeks				
arithmetic mean (standard error)	21.4 (± 1.4)	23.8 (± 1.0)	25.5 (± 0.0)	21.3 (± 2.7)

End point values	Arm A Scarring	Arm A Cutis laxa	Arm B Scarring	Arm B Cutis laxa
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	36	10	10
Units: weeks				
arithmetic mean (standard error)	22.3 (± 1.3)	22.8 (± 1.2)	21.3 (± 3.1)	25.5 (± 0.0)

Statistical analyses

Statistical analysis title	Log Rank (Mantel-Cox)
Comparison groups	Placebo v Arm A
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.869
Method	Logrank

Statistical analysis title	Log Rank (Mantel-Cox)
Comparison groups	Arm A Scarring v Arm B Scarring

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.515
Method	Logrank

Statistical analysis title	Log Rank (Mantel-Cox)
Comparison groups	Arm A Cutis laxa v Arm B Cutis laxa
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.334
Method	Logrank

Statistical analysis title	Log Rank (Mantel-Cox)
Comparison groups	Arm A Scarring ADSC v Arm B Scarring ADSC
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.903
Method	Logrank

Statistical analysis title	Log Rank (Mantel-Cox)
Comparison groups	Arm A Scarring SVF v Arm B Scarring SVF
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.454
Method	Logrank

Statistical analysis title	Log Rank (Mantel-Cox)
Comparison groups	Arm A Cutis laxa ADSC v Arm B Cutis laxa ADSC
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.757
Method	Logrank

Statistical analysis title	Log Rank (Mantel-Cox)
Comparison groups	Arm A ADSC v Arm B ADSC
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.918
Method	Logrank

Statistical analysis title	Log Rank (Mantel-Cox)
Comparison groups	Arm A SVF v Arm B SVF
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.869
Method	Logrank

Statistical analysis title	Univariate Cox hazard models
Comparison groups	Arm A v Placebo
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.877
Method	Regression, Cox

Statistical analysis title	Univariate Cox hazard models
Comparison groups	Arm B Scarring v Arm A Scarring
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.546
Method	Regression, Cox

Statistical analysis title	Univariate Cox hazard models
Comparison groups	Arm A Cutis laxa v Arm B Cutis laxa
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	Regression, Cox

Statistical analysis title	Univariate Cox hazard models
Comparison groups	Arm A Scarring ADSC v Arm B Scarring ADSC
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.909
Method	Regression, Cox

Statistical analysis title	Univariate Cox hazard models
Comparison groups	Arm B Scarring SVF v Arm A Scarring SVF
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.489
Method	Regression, Cox

Statistical analysis title	Univariate Cox hazard models
Comparison groups	Arm B Cutis laxa ADSC v Arm A Cutis laxa ADSC
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.765
Method	Regression, Cox

Statistical analysis title	Univariate Cox hazard models
Comparison groups	Arm B ADSC v Arm A ADSC
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.922
Method	Regression, Cox

Statistical analysis title	Univariate Cox hazard models
Comparison groups	Arm A SVF v Arm B SVF

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.876
Method	Regression, Cox

Statistical analysis title	Multivariate Cox hazard models
Comparison groups	Arm A v Placebo
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.878
Method	Regression, Cox

Statistical analysis title	Multivariate Cox hazard models
Comparison groups	Arm B Scarring v Arm A Scarring
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.557
Method	Regression, Cox

Statistical analysis title	Multivariate Cox hazard models
Comparison groups	Arm A Cutis laxa v Arm B Cutis laxa
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	Regression, Cox

Secondary: Change in the assessment of skin lesions	
End point title	Change in the assessment of skin lesions

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Cutis laxa SVF	Arm A Cutis laxa ADSC	Arm A Scarring ADSC
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	17	19	19
Units: scale				
arithmetic mean (standard deviation)	-9.00 (± 13.44)	-9.41 (± 17.91)	-6.26 (± 19.10)	-10.95 (± 12.34)

End point values	Arm B Cutis laxa ADSC	Arm B Scarring ADSC	Arm B Cutis laxa SVF	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	5	5	5
Units: scale				
arithmetic mean (standard deviation)	-11.40 (± 11.39)	-11.80 (± 13.12)	-4.40 (± 5.77)	-19.80 (± 20.03)

End point values	Arm A ADSC	Arm A SVF	Arm B ADSC	Arm B SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38	35	10	10
Units: scale				
arithmetic mean (standard deviation)	-8.61 (± 16.04)	-9.20 (± 15.53)	-11.60 (± 11.59)	-12.10 (± 16.09)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the thickness of the scar on ultrasound

End point title	Change in the thickness of the scar on ultrasound

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	19	5	5
Units: mm				
arithmetic mean (standard deviation)	0.03 (± 0.88)	-0.08 (± 0.82)	0.50 (± 0.55)	0.13 (± 0.70)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the thickness of the subcutaneous tissue on ultrasound

End point title	Change in the thickness of the subcutaneous tissue on ultrasound

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	19	5	5
Units: mm				
arithmetic mean (standard deviation)	-1.45 (± 11.43)	3.18 (± 10.58)	-2.22 (± 8.40)	0.55 (± 1.17)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the color of the scar as assessed by the investigator

End point title	Change in the color of the scar as assessed by the investigator

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-0.88 (± 0.60)	-1.32 (± 0.67)	-1.00 (± 0.71)	-1.20 (± 0.45)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the appearance of the scar as assessed by the investigator

End point title	Change in the appearance of the scar as assessed by the investigator

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-0.41 (± 0.51)	-0.42 (± 0.51)	-0.20 (± 0.45)	-0.60 (± 0.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the prominence of the scar as assessed by the investigator

End point title	Change in the prominence of the scar as assessed by the investigator

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-0.88 (± 0.93)	-0.95 (± 0.85)	-0.60 (± 0.55)	-1.20 (± 0.84)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in scar deformation as assessed by the investigator

End point title	Change in scar deformation as assessed by the investigator

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-1.29 (± 0.59)	-1.21 (± 0.63)	-0.80 (± 0.45)	-0.60 (± 0.89)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the structure of the scar as assessed by the investigator

End point title	Change in the structure of the scar as assessed by the investigator

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-1.06 (± 0.75)	-1.26 (± 0.65)	-1.00 (± 0.71)	-1.60 (± 0.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in pain as assessed by the patient

End point title	Change in pain as assessed by the patient

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-0.06 (± 0.42)	-0.16 (± 0.83)	0.00 (± 0.00)	-1.20 (± 1.64)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in itching as assessed by the patient

End point title	Change in itching as assessed by the patient

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-0.11 (± 0.68)	-0.21 (± 0.79)	0.00 (± 0.00)	-0.80 (± 1.30)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the color of the scar as assessed by the patient

End point title	Change in the color of the scar as assessed by the patient

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-1.83 (± 1.50)	-1.58 (± 1.50)	-1.60 (± 3.36)	-3.00 (± 1.58)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in scar thickness as assessed by the patient

End point title	Change in scar thickness as assessed by the patient

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-1.89 (± 1.60)	-1.11 (± 1.52)	-1.80 (± 0.84)	-2.60 (± 2.30)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in scar irregularity as assessed by the patient

End point title	Change in scar irregularity as assessed by the patient

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Scarring SVF	Arm A Scarring ADSC	Arm B Scarring ADSC	Arm B Scarring SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-1.61 (± 1.29)	-1.05 (± 1.61)	-1.40 (± 1.14)	-2.80 (± 2.17)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in skin thickness on ultrasound

End point title	Change in skin thickness on ultrasound

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Cutis laxa SVF	Arm A Cutis laxa ADSC	Arm B Cutis laxa ADSC	Arm B Cutis laxa SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	19	5	5
Units: mm				
arithmetic mean (standard deviation)	0.25 (± 0.25)	0.22 (± 0.17)	0.24 (± 0.14)	0.37 (± 0.28)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the thickness of the subcutaneous tissue on ultrasound

End point title	Change in the thickness of the subcutaneous tissue on ultrasound

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Cutis laxa SVF	Arm A Cutis laxa ADSC	Arm B Cutis laxa ADSC	Arm B Cutis laxa SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	19	5	5
Units: mm				
arithmetic mean (standard deviation)	0.54 (± 1.14)	0.74 (± 0.82)	0.75 (± 1.02)	1.13 (± 0.59)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the degradation of subcutaneous tissue

End point title	Change in the degradation of subcutaneous tissue

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, week 4-5, week 8-9, week 24-27 and on early termination of the study

End point values	Arm A Cutis laxa SVF	Arm A Cutis laxa ADSC	Arm B Cutis laxa ADSC	Arm B Cutis laxa SVF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	19	5	5
Units: scale				
arithmetic mean (standard deviation)	-1.12 (± 0.78)	-1.16 (± 0.90)	-1.00 (± 1.22)	-1.40 (± 0.89)

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of the safety of the application method by assessment of adverse reactions

End point title	Evaluation of the safety of the application method by assessment of adverse reactions

End point description:

End point type	Secondary

End point timeframe:

Assessments were performed on day 0, day 0 +1 day, day 6-12, week 2, week 4-5, week 6, week 8-9, week 10, week 24-27 and on early termination of the study

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	94			
Units: number od adverse reactions	150			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Assessment of adverse events was conducted from day 0 to the end of clinical trial (week 24-27).

Adverse event reporting additional description:

Assessments were performed on day 0, day 0 +1 day, day 6-12, week 2, week 4-5, week 6, week 8-9, week 10, week 24-27 and on early termination of the study

Assessment type	Systematic

Dictionary used

Dictionary name	other
Dictionary version	0

Reporting groups

Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 94 (1.06%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Blood pressure increased	Additional description: Patient 2ABC01016 experienced SAE that was hospitalization for increased blood pressure. Patient recovered completely. In the investigator's opinion, it was not related to the test product, but administration of the product was discontinued.		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 94 (58.51%)		
General disorders and administration site conditions			
Swelling	Additional description: Swelling after mesotherapy		
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	7		
Erythema	Additional description: Skin erythema after mesotherapy		

subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	9		
Dry skin	Additional description: Hand skin roughness or dryness after mesotherapy		
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	5		
Skin injury	Additional description: Bruising hand skin at the application site		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Skin irritation	Additional description: Itching of the hand skin at the application site		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Skin sensitisation	Additional description: Paresthesia after liposuction		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Pain	Additional description: Pain associated with liposuction		
subjects affected / exposed	13 / 94 (13.83%)		
occurrences (all)	14		
Blood pressure increased	Additional description: Increased blood pressure		
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
Abdominal pain	Additional description: Stabbing pain in the lower left abdominal quadrant		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Throat irritation	Additional description: Sore throat		
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
Rhinitis	Additional description: Watery rhinitis		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Headache	Additional description: Headache		
subjects affected / exposed	13 / 94 (13.83%)		
occurrences (all)	25		
Tremor	Additional description: Symptoms of tremor combined with an episode of increased blood pressure (160/98)		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		

Pharyngitis	Additional description: Acute pharyngitis		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Immune system disorders			
Allergy to plants	Additional description: Birch pollen allergy		
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Allergic respiratory disease	Additional description: Respiratory allergy		
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	6		
Eye allergy	Additional description: Itching and redness of the conjunctiva of both eyes of an allergic nature		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Menstruation irregular	Additional description: Occurrence of menstrual bleeding after an 8-month break		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Menopausal symptoms	Additional description: Perimenopausal symptoms		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Respiratory tract infection	Additional description: Infection of the upper or lower respiratory tract, common cold		
subjects affected / exposed	16 / 94 (17.02%)		
occurrences (all)	18		
Sinusitis	Additional description: Inflammation of the paranasal sinuses		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Cough	Additional description: Cough		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Asthma	Additional description: Asthmatic symptoms (exacerbation of periodically occurring dyspnoea in the spring)		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Nervous system disorders			

Migraine	Additional description: Migraine headache		
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Oedema peripheral	Additional description: Painless swelling of lower legs		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Iron deficiency	Additional description: Low serum iron levels (up to 55 mcg/ml)		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Otitis media acute	Additional description: Acute otitis media		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Ear pain	Additional description: Ear pain		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Eye disorders			
Lacrimation increased	Additional description: Lacrimation acompanied by a runny nose		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Conjunctivitis	Additional description: Conjunctivitis of both eyes		
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Gastrointestinal disorders			
Gastric pH increased	Additional description: Gastric hyperacidity		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Vitiligo	Additional description: Vitiligo in the place of the scar on the hand after laser treatment		

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Inflammation	Additional description: Nonspecific inflammation of the soft tissues of the hands with massive swelling; inflammatory lump on the forearm		
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	4		
Scar pain	Additional description: Pain in the scar area		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Haemorrhage subcutaneous	Additional description: Subcutaneous hemorrhage under the eye		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Urticaria	Additional description: Acute urticaria		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Skin reaction	Additional description: Skin allergy		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism	Additional description: Hypothyroidism		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Ankle deformity	Additional description: Right ankle sprain		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Back pain	Additional description: Spine pain		
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Tooth fracture	Additional description: Fracture in the root of the lower left IV tooth		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Pain in extremity	Additional description: Lower limb pain in the area of the left shin; pain in the left shoulder area; hip pain		
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Finger deformity	Additional description: Injury of fourth finger of the right hand		

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Formication	Additional description: Formication and numbness of both hands radiating to the elbows		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Infections and infestations			
Viral infection	Additional description: Shingles		
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	4		
Bite	Additional description: Tick bite		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported