Clinical trial results:
Treatment of hypertrophic scars using needle-free jet-injection of triamcinolone and 5-Fluorouracile: a prospective, controlled, randomized, single-blinded split-lesion trial.

Summary

EudraCT number	2019-001066-15
Trial protocol	DK
Global end of trial date	17 March 2020

Results information

Result version number	v1 (current)
This version publication date	27 November 2021
First version publication date	27 November 2021

Trial information

Trial identification

Sponsor protocol code	LR19912019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	De Videnskabsetiske Komiteer for Region Hovedstade: H-19024719

Notes:

Sponsors

Sponsor organisation name	Merete Hædersdal
Sponsor organisation address	Nielsine Nielsens Vej 17, opgang 9, 2 sal, Copenhagen NV, Denmark, 2400
Public contact	Department of Dermatology, Bispebjerg Hospital, 0045 3635000, Katrine.togsverd-bo@regionh.dk
Scientific contact	Department of Dermatology, Bispebjerg Hospital, 0045 3635000, Katrine.togsverd-bo@regionh.dk

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	20 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 March 2020
Global end of trial reached?	Yes
Global end of trial date	17 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- Blinded, on-site, clinical evaluation of mean change in HTS height following jet-injections with TAC+5-FU at baseline and 4 weeks (+/- 5 days) after intervention, by Vancouver Scar Scale height (VSSheight).

- Blinded, on-site, clinical evaluation of mean change in HTS appearance following jet-injections with TAC+5-FU at baseline and 4 weeks (+/- 7 days) after intervention, by full Vancouver Scar Scale (VSStotal).

- Mean change in blinded, evaluation of clinical photos by off-site, clinical experts. evaluation of clinical photos of treated scar site, at baseline and 4 weeks (+/- 7 days) after intervention, and treated vs. untreated scar sites 4 weeks (+/- 7 days) from intervention, using the Visual Analogue Scale (VAS)

Protection of trial subjects:

All intrested patients was invited to a preliminary informational screening visit at which they recceived comprehensive oral information on the study by the primary investigator, Merete Hædersdal, and written information was handed out. All Patients was informed both verbally and in written form about risks and possible side-effects of all tests/treatments offered. The meeting took place in a separate office to ensure a safe and calm environment. The patients was specifically informed that they can bring one or more assessors to all meetings and interventions if they so choose. Each patient was evaluated by the investigator to assess the suitability of entering the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2019
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	Denmark: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment to begin and study interventions 1. September 2019. Last patient last visit: 1 march. 2020. End of study: 15. march 2020. All potential patients was recruited from the Department of Dermatology, Bispebjerg Hospital

Pre-assignment

Screening details:

14 patients was excluted due to: History of, or presenting with a keloid scar / Use of topical treatment in the last 6 months and lack of willingness to refrain use during the trial as topical treatment / Anti Coagulatory Treatment.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Assessor, Investigator[2]

Blinding implementation details:

Included HTS will be split into two halves. Each scar half will be assigned to jet-injection treatment or serve as untreated control according to a balanced randomization. Randomization will be conducted with consecutively numbered, closed, non- transparent envelopes containing a computer-generated allocation. The envelopes will be prepared by a third party to ensure allocation concealment, taken to use in a numeric order and opened just before the jet-injection treatment.

Arms

Are arms mutually exclusive?	No
Arm title	Untreated.

Arm description:

Half of the HTS (scar) that was allocated to untreated / control did now reccive the active treatment.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment

Arm description:

The half of the scar allocated to treatment.

Arm type	Experimental
Investigational medicinal product name	Triamcinolone acetonide
Investigational medicinal product code	Triamcinolone acetonide
Other name	Kenalog
Pharmaceutical forms	Suspension for injection in multidose container
Routes of administration	Subdermal use

Dosage and administration details:

1 part TAC 10 or 40 mg/ml (Kenalog®, Bristol-Myers Squibb, Denmark) and 9 parts 5-FU 50 mg/mg (Fluorouracil "Accord", Accord Healthcare Limited, England). Strength of TAC will be clinically based on the HTS and the atrophic potential and/or anatomical location. A maximum of 80 mg TAC or 100 mg 5-FU will be used in the treatment session

Investigational medicinal product name	Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in multidose container
Routes of administration	Subdermal use

Dosage and administration details:

1 part TAC 10 or 40 mg/ml (Kenalog®, Bristol-Myers Squibb, Denmark) and 9 parts 5-FU 50 mg/mg

(Fluorouracil "Accord", Accord Healthcare Limited, England). Strength of TAC will be clinically based on the HTS and the atrophic potential and/or anatomical location. A maximum of 80 mg TAC or 100 mg 5-FU will be used in the treatment session

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: Included HTS will be split into two halves. Each scar half will be assigned to jet-injection treatment or serve as untreated control according to a balanced randomization. The scar part located the furthest to the left (from the patient's perspective) is referred to as lesion 1, the scar part further to the right as lesion 2. If the scar is vertically arranged, the upper wound part is referred to as lesion 1 and the lower one as lesion 2. Lesion 1 and 2 will be randomized for jet-injection treat

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Included HTS will be split into two halves. Each scar half will be assigned to jet-injection treatment or serve as untreated control according to a balanced randomization. The scar part located the furthest to the left (from the patient's perspective) is referred to as lesion 1, the scar part further to the right as lesion 2. If the scar is vertically arranged, the upper wound part is referred to as lesion 1 and the lower one as lesion 2. Lesion 1 and 2 will be randomized for jet-injection treat

Number of subjects in period 1	Untreated.	Treatment
Started	20	20
Completed	20	20

Baseline characteristics

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	20	20	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
age range			
Units: years			
arithmetic mean	30		
standard deviation	± 17	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	5	5	

End points

End points reporting groups

Reporting group title	Untreated.
Reporting group description:	
Half of the HTS (scar) that was allocated to untreated / control did now reccive the active treatment.	
Reporting group title	Treatment
Reporting group description:	
The half of the scar allocated to treatment.	

Primary: Vancouver Scar Scale height (VSSheight)

End point title	Vancouver Scar Scale height (VSSheight)
End point description:	
linded, on-site, clinical evaluation of mean change in HTS appearance following jet- injections with TAC+5-FU at baseline and 4 weeks (+/- 7 days) after intervention, by full Vancouver Scar Scale (VSStotal), to evaluate the potential clinical effect on the scar parameters: vascularity, pigmentation, pliability and height	
End point type	Primary
End point timeframe:	
At baseline and follow-up 4 weeks (+/- 7 days)	

End point values	Untreated.	Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: 0-14				
number (not applicable)				
vascularity	1	1		
pigmentation	1	1		
pliability	1	1		
height	6	5		

Statistical analyses

Statistical analysis title	Wilcoxon signed-rank test
Statistical analysis description:	
A sample size of 16 patients provided 90% power to detect a clinical change of 50% in VSS height with an α = 0.05. A 20% attrition rate against dropout was chosen, and 20 patients were included. Descriptive statistics and tables are presented as medians or means with interquartile ranges (IQR) and standard deviations (SD), unless otherwise stated. Wilcoxon signed-rank test was used to compare baseline and follow-up data. Level of significance = $p<0.05$. Statistical analysis was performed using SP	
Comparison groups	Untreated. v Treatment

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs are reported within 24 hours to sponsor-investigator Merete Hædersdal. At the end of the trial, a final report with all AEs, ARs, SAEs and SUSARs is handed to the Danish Health and Medicine Authority and the Regional Committee on Health Research Ethi

Adverse event reporting additional description:

The investigators are responsible for routine assessments of AEs and ARs. All clinical complaints, symptoms or signs that meet AE or AR definitions will be documented in the study record and the participant's medical record.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Adverse events

Reporting group description:

Three patients experienced mild AE.

Serious adverse events	Adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)		
Skin and subcutaneous tissue disorders			
punctate defects	Additional description: Three patients reported punctate defects at one of the injection sites in treated part of the scar; all but one were resolved at 4-weeks follow-up.		
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		

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