Clinical trial results:
Treatment of photodamaged skin of the décolleté with fractional laser, radio-frequency microneedling, and photodynamic therapy

Summary

EudraCT number	2018-000189-12
Trial protocol	DK
Global end of trial date	18 December 2018

Results information

Result version number	v1 (current)
This version publication date	12 July 2020
First version publication date	12 July 2020

Trial information

Trial identification

Sponsor protocol code	LS2018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03573076
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bispebjerg University Hospital
Sponsor organisation address	Nielsine Nielsens Vej 17, Opgang 9, Copenhagen, Denmark, 2400
Public contact	Dermatologisk forskningsafdeling, Bispebjerg Hospital, 0045 41184700, merete.haedersdal@regionh.dk
Scientific contact	Dermatologisk forskningsafdeling, Bispebjerg Hospital, 0045 41184700, merete.haedersdal@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	01 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2018
Global end of trial reached?	Yes
Global end of trial date	18 December 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

In patients with photodamaged skin in the décolleté region, the objective is to investigate a non-ablative fractional thulium laser and a radio-frequency microneedling device as pre-treatment approaches for combination photodynamic therapy in treatment of photoaged skin and actinic keratoses.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 2018
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: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	4
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from the Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark and private dermatological practices in Copenhagen, Denmark.

Pre-assignment

Screening details:

Patients were screened if they seemed to meet inclusion criteria.

Period 1

Period 1 title	Baseline evaluation
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Arm title	Evaluation
Arm description: -	
Arm type	Evaluation
Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:

Normal saline

Number of subjects in period 1	Evaluation
Started	12
Completed	12

Period 2

Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No

Arm title	Thulium laser plus photodynamic therapy
Arm description: TL + PDT	
Arm type	Experimental
Investigational medicinal product name	Metyl aminolevulinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use
Dosage and administration details: Methyl aminolevulinate 2% creme was applied once with and without thulium laser pre-treatment.	
Arm title	Thulium laser
Arm description: TL alone	
Arm type	Experimental
Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use
Dosage and administration details: Normal saline	
Arm title	Photodynamic therapy
Arm description: PDT alone	
Arm type	Experimental
Investigational medicinal product name	Metyl aminolevulinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use
Dosage and administration details: Methyl aminolevulinate 2% creme was applied once	
Arm title	Control curettage
Arm description: Only lesion-specific (AK) curettage	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Thulium laser plus photodynamic therapy	Thulium laser	Photodynamic therapy
Started	12	12	12
Completed	12	12	12

Number of subjects in period 2	Control curettage

Started	12
Completed	12

Period 3

Period 3 title	Evaluation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Arms

Are arms mutually exclusive?	No
Arm title	Thulium laser plus photodynamic therapy

Arm description:
TL + PDT

Arm type	Experimental
Investigational medicinal product name	Metyl aminolevulinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:
Methyl aminolevulinate 2% creme was applied once with and without thulium laser pre-treatment.

Arm title	Thulium laser

Arm description:
TL alone

Arm type	Experimental
Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:
Normal saline

Arm title	Photodynamic therapy

Arm description:
PDT alone

Arm type	Experimental
Investigational medicinal product name	Metyl aminolevulinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Methyl aminolevulinate 2% creme was applied once

Arm title	Control curettage

Arm description:

Only lesion-specific (AK) curettage

Arm type	No intervention

No investigational medicinal product assigned in this arm

Notes:

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

Justification: The nature of the treatments do not allow the treating physician to be blinded. A separate assessor (physician) conducted the single-blind analyses.

Number of subjects in period 3	Thulium laser plus photodynamic therapy	Thulium laser	Photodynamic therapy
Started	12	12	12
Completed	12	12	12

Number of subjects in period 3	Control curettage
Started	12
Completed	12

Baseline characteristics

Reporting groups

Reporting group title	Baseline evaluation

Reporting group description: -

Reporting group values	Baseline evaluation	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
Age continuous Units: years			
median	69		
full range (min-max)	54 to 76	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	0	0	

Subject analysis sets

Subject analysis set title	Efficacy
Subject analysis set type	Full analysis

Subject analysis set description:
Efficacy

Reporting group values	Efficacy		
Number of subjects	12		
Age categorical Units: Subjects			
Age continuous Units: years			
median	69		
full range (min-max)	54 to 76		
Gender categorical Units: Subjects			
Female	12		
Male	0		

End points

End points reporting groups

Reporting group title	Evaluation
Reporting group description: -	
Reporting group title	Thulium laser plus photodynamic therapy
Reporting group description: TL + PDT	
Reporting group title	Thulium laser
Reporting group description: TL alone	
Reporting group title	Photodynamic therapy
Reporting group description: PDT alone	
Reporting group title	Control curettage
Reporting group description: Only lesion-specific (AK) curettage	
Reporting group title	Thulium laser plus photodynamic therapy
Reporting group description: TL + PDT	
Reporting group title	Thulium laser
Reporting group description: TL alone	
Reporting group title	Photodynamic therapy
Reporting group description: PDT alone	
Reporting group title	Control curettage
Reporting group description: Only lesion-specific (AK) curettage	
Subject analysis set title	Efficacy
Subject analysis set type	Full analysis
Subject analysis set description: Efficacy	

Primary: Clinical improvement in photodamage

End point title	Clinical improvement in photodamage
End point description:	
End point type	Primary
End point timeframe: Final evaluation (12 weeks)	

End point values	Thulium laser plus photodynamic therapy	Thulium laser	Photodynamic therapy	Control curettage
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: 0-4				
median (inter-quartile range (Q1-Q3))	1.000 (1.000 to 1.500)	1.000 (0.500 to 1.500)	0.500 (-0.875 to 1.250)	0.000 (-0.500 to 0.100)

Statistical analyses

Statistical analysis title	TL-PDT compared with control
Comparison groups	Control curettage v Thulium laser plus photodynamic therapy
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)

Statistical analysis title	TL compared with control
Comparison groups	Thulium laser v Control curettage
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)

Statistical analysis title	PDT compared with control
Comparison groups	Photodynamic therapy v Control curettage
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.063
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)

Secondary: Treatment effect on AK lesions

End point title	Treatment effect on AK lesions

End point description:

End point type	Secondary

End point timeframe:

Final evaulation (12 weeks)

End point values	Thulium laser plus photodynamic therapy	Thulium laser	Photodynamic therapy	Control curettage
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: 100				
median (inter-quartile range (Q1-Q3))	100 (90 to 100)	90 (56 to 100)	82 (70 to 100)	55 (28 to 100)

Statistical analyses

Statistical analysis title	All interventions compared
Comparison groups	Thulium laser plus photodynamic therapy v Thulium laser v Photodynamic therapy v Control curettage
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.464
Method	Kruskal-wallis
Parameter estimate	Median difference (final values)

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Until final evaluation (12 weeks)	
Assessment type	Systematic

Dictionary used	
Dictionary name	ICD
Dictionary version	10

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Photodynamic therapy is well-known and safe. The laser treatment was conducted expertly at our unversity hosptial, and neither expected nor saw any adverse events.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Please see published article for a discussion on limitations.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31788828