



Clinical trial results:

Pretreatment with ablative fractional laser and microdermabrasion before photodynamic therapy for actinic keratoses in field-cancerized skin

Summary

EudraCT number	2015-002331-18
Trial protocol	DK
Global end of trial date	01 October 2018

Results information

Result version number	v1 (current)
This version publication date	21 June 2022
First version publication date	21 June 2022

Trial information

Trial identification

Sponsor protocol code	48739
-----------------------	-------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bispebjerg Hospital, Department of Dermatology
Sponsor organisation address	Nielsine Nielsensvej 9, Copenhagen, Denmark,
Public contact	Katrine Togsverd-Bo, Bispebjerg Hospital, Department of dermatology, 0045 53539178, katrinetogsverd@hotmail.com
Scientific contact	Katrine Togsverd-Bo, Bispebjerg Hospital, Department of dermatology, 0045 53539178, katrinetogsverd@hotmail.com

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	07 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 May 2018
Global end of trial reached?	Yes
Global end of trial date	01 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Comparison of treatment efficacy of pretreatment with ablative fractional laser versus microdermabrasion combined with large-area photodynamic with methyl aminolevulinate for actinic keratoses

Protection of trial subjects:

Patients were followed up closely and were offered pain relief for topical interventions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 May 2016
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	Denmark: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	3
From 65 to 84 years	14
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

patients were recruited from the hospitals outpatient clinic

Pre-assignment

Screening details:

Patients were to have clinical AKs in two side-by-side skin areas within the same anatomic location on the face, scalp, or chest with at least 5 AKs.

Patients with porphyria, infiltrating tumors in treatment areas, pregnancy, lactation, or AK treatment in study areas 4 weeks before inclusion

Period 1

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

Blinding implementation details:

Blinded clinical evaluation of primary end point (AK)

Arms

Are arms mutually exclusive?	No
Arm title	AFL- PDT

Arm description:

Ablative fractional laser combined with daylight photodynamic therapy

Arm type	Active comparator
Investigational medicinal product name	methyl aminolevulinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream + pessary
Routes of administration	Topical use

Dosage and administration details:

MAL cream applied in 0.3-0.5 mm thickness to the treatment area. Up to 1 g.

One treatment

Arm title	MD PDT
------------------	--------

Arm description:

Microdermabrasion pretreatment performed prior to photodynamic therapy

Arm type	Experimental
Investigational medicinal product name	methyl aminolevulinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream + pessary
Routes of administration	Topical use

Dosage and administration details:

MAL cream applied in 0.3-0.5 mm thickness to the treatment area. Up to 1 g.

One treatment

Number of subjects in period 1	AFL- PDT	MD PDT
Started	18	18
Completed	18	18

Baseline characteristics

Reporting groups

Reporting group title	overall trial
-----------------------	---------------

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	18	18	
Age categorical			
Units: Subjects			
Adults (18-64 years)	3	3	
From 65-84 years	14	14	
85 years and over	1	1	
Age continuous			
Units: years			
median	73		
full range (min-max)	58 to 87	-	
Gender categorical			
Units: Subjects			
male	12	12	
female	6	6	
Fitzpatrick skin type			
Units: Subjects			
Fitzpatrick skin type	18	18	

Subject analysis sets

Subject analysis set title	AK response
----------------------------	-------------

Subject analysis set type	Intention-to-treat
---------------------------	--------------------

Subject analysis set description:

18 participants were included as a preemptive measure against drop-out. AK clearance rates and patientreported pain was analyzed using paired t-tests after Shapiro-Wilk test confirmed normal distribution.

Reporting group values	AK response		
Number of subjects	18		
Age categorical			
Units: Subjects			
Adults (18-64 years)	3		
From 65-84 years	14		
85 years and over	1		
Age continuous			
Units: years			
median	73		
full range (min-max)	58 to 87		
Gender categorical			
Units: Subjects			
male	12		

female	6		
--------	---	--	--

Fitzpatrick skin type			
Units: Subjects			
Fitzpatrick skin type	18		

End points

End points reporting groups

Reporting group title	AFL- PDT
Reporting group description: Ablative fractional laser combined with daylight photodynamic therapy	
Reporting group title	MD PDT
Reporting group description: Microdermabrasion pretreatment performed prior to photodynamic therapy	
Subject analysis set title	AK response
Subject analysis set type	Intention-to-treat
Subject analysis set description: 18 participants were included as a preemptive measure against drop-out. AK clearance rates and patient-reported pain was analyzed using paired t-tests after Shapiro-Wilk test confirmed normal distribution.	

Primary: AK lesion response

End point title	AK lesion response
End point description: s AK complete response (CR) rate, defined as the number of cleared AKs at 3-months follow-up, divided by AK number at baseline. Two blinded evaluators (E.W. and C.B.) assessed areas visually and by palpation.	
End point type	Primary
End point timeframe: 3 months after treatment	

End point values	AFL- PDT	MD PDT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: AK lesions				
AK CR	81	60		

Statistical analyses

Statistical analysis title	paired t test
Statistical analysis description: paired test as intra-individual design	
Comparison groups	AFL- PDT v MD PDT
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided

Secondary: local skin response

End point title	local skin response
-----------------	---------------------

End point description:

redness, edema, flaking, sores, crusting, pustules and erosions. Each parameter was graded on 4-point severity scale (0-3) representing none, mild, moderate and severe. A total composite score reflecting overall LSR severity was then calculated based on the sum of all parameters

End point type	Secondary
----------------	-----------

End point timeframe:

Days 1-2, 3-6, 7-14 and Weeks 12-15,

End point values	AFL- PDT	MD PDT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: categorical severity score				
daya 1-2	6	3		
day 3-5	7	4		
day 7-14	2	0		
weeks 12-15	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Photodamage improvement

End point title	Photodamage improvement
-----------------	-------------------------

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

improvement weeks 12-15 from baseline

End point values	AFL- PDT	MD PDT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: photodamage severity				
photodamage improvement	1	0		

Statistical analyses

Statistical analysis title	Wilcoxon signed rank test
Comparison groups	AFL- PDT v MD PDT
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: dyspigmentation

End point title	dyspigmentation
End point description:	hyper-, or hypopigmentation during the study period graded on 4-point categorical scale
End point type	Secondary
End point timeframe:	week 12-15

End point values	AFL- PDT	MD PDT	AK response	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	18	18	
Units: dyspigmentation severity				
hypopigmentation	18	18	18	
hyperpigmentation	18	18	18	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

15 weeks after study inclusion

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	10
--------------------	----

Reporting groups

Reporting group title	All subjects
-----------------------	--------------

Reporting group description: -

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0.5 %

Non-serious adverse events	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 18 (16.67%)		
Skin and subcutaneous tissue disorders			
Skin infection	Additional description: Local skin infection corresponding to treatment area		
subjects affected / exposed	3 / 18 (16.67%)		
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